```
=> d his ful

     (FILE 'HOME' ENTERED AT 16:26:45 ON 08 DEC 2005)

     FILE 'HCAPLUS' ENTERED AT 16:26:50 ON 08 DEC 2005
L1             1 SEA ABB=ON  PLU=ON  US200!-798470/APPS
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 16:27:08 ON 08 DEC 2005
L2            29 SEA ABB=ON  PLU=ON  (103775-10-6/BI OR 111223-26-8/BI OR
                 111902-57-9/BI OR 127420-24-0/BI OR 140369-78-4/BI OR 142695-08
                 -7/BI OR 182176-67-6/BI OR 182176-70-1/BI OR 182176-83-6/BI OR
                 39698-78-7/BI OR 62571-86-2/BI OR 74258-86-9/BI OR 75847-73-3/B
                 I OR 76420-72-9/BI OR 76547-98-3/BI OR 82768-85-2/BI OR
                 82834-16-0/BI OR 83435-66-9/BI OR 83647-97-6/BI OR 85441-61-8/B
                 I OR 86541-75-5/BI OR 87333-19-5/BI OR 87679-37-6/BI OR
                 88768-40-5/BI OR 89371-37-9/BI OR 9015-82-1/BI OR 95153-31-4/BI
                  OR 95399-71-6/BI OR 98048-97-6/BI)

     FILE 'HCAPLUS' ENTERED AT 16:27:13 ON 08 DEC 2005
L3             1 SEA ABB=ON  PLU=ON  L1 AND L2
                 D IALL HITSTR
                 E INFLAMMATORY BOWEL DISEASE/CT
                 E E3+ALL
                 E E2+ALL
L4          7752 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) INFLAMMATORY"+PFT/C
                 T
                 E SHORT BOWEL SYNDROME/CT
                 E E4+ALL
                 E E2+ALL
L5           261 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) SHORT BOWEL
                 SYNDROME"+PFT/CT
                 E CROHNS DISEASE/CT
                 E E1+ALL
                 E E2+ALL
L6             4 SEA ABB=ON  PLU=ON  "INFLAMMATION (L) CROHN'S DISEASE"+PFT/CT
                 E CROHNS DISEASE/CT
                 E E1+ALL
                 E E3+ALL
L7             4 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) CROHN'S"+PFT/CT
                 E CELIAC DISEASE/CT
                 E E3+ALL
L8          2349 SEA ABB=ON  PLU=ON  CELIAC DISEASE+PFT/CT
                 E ULCERATIVE COLITIS/CT
                 E E3+ALL
                 E E2+ALL
L9          4545 SEA ABB=ON  PLU=ON  "INFLAMMATION (L) ULCERATIVE COLITIS"+PFT/C
                 T
                 E ULCERATIVE COLITIS/CT
                 E E3+ALL
                 E E3+ALL
L10         4544 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) ULCERATIVE
                 COLITIS"+PFT/CT
                 E STOMACH ULCERS/CT
                 E ULCER/CT
                 E STOMACH, DISEA/CT
                 E E25+ALL
L11         2302 SEA ABB=ON  PLU=ON  "STOMACH, DISEASE (L) ULCER"+PFT/CT
                 E DIVERTICULITIS/CT
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                E E3+ALL
                E E2+ALL
L12         130 SEA ABB=ON  PLU=ON  "INFLAMMATION (L) DIVERTICULITIS"+PFT/CT
                E DIVERTICULITIS/CT
                E E3+ALL
                E E3+ALL
L13         130 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) DIVERTICULITIS"+PFT
                /CT
                E POUCHITIS/CT
                E PROCTITIS/CT
                E E3+ALL
                E E2+ALL
L14         199 SEA ABB=ON  PLU=ON  "INFLAMMATION (L) RECTAL"+PFT/CT
                E PROCTITIS/CT
                E E3+ALL
                E E3+ALL
L15         177 SEA ABB=ON  PLU=ON  "INTESTINE, DISEASE (L) RECTUM, INFLAMMATIO
                N"+PFT/CT
                E CHRONIC DIARRHEA/CT
                E DIARRHEA/CT
                E E3+ALL
L16          78 SEA ABB=ON  PLU=ON  DIARRHEA+PFT/CT(L)CHRONIC
L17       21694 SEA ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10
                OR L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR INFLAMMATORY
                BOWEL OR SHORT BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR
                CELIAC DISEAS? OR ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR
                DIVERTICULITIS OR POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA

                E ANGIOTENSIN CONVERTING ENZYME

     FILE 'REGISTRY' ENTERED AT 16:39:36 ON 08 DEC 2005
                E ALACEPRIL/CN
L18             1 SEA ABB=ON  PLU=ON  ALACEPRIL/CN
L19             1 SEA ABB=ON  PLU=ON  BENAZEPRIL/CN
L20             1 SEA ABB=ON  PLU=ON  LOTENSIN/CN
L21             1 SEA ABB=ON  PLU=ON  CAPTOPRIL/CN
L22             1 SEA ABB=ON  PLU=ON  CILAZAPRIL/CN
L23             1 SEA ABB=ON  PLU=ON  CERANAPRIL
L24             1 SEA ABB=ON  PLU=ON  DELAPRIL/CN
L25             1 SEA ABB=ON  PLU=ON  ENALAPRIL/CN
L26             1 SEA ABB=ON  PLU=ON  ENALAPRILAT/CN
L27             1 SEA ABB=ON  PLU=ON  FOSINOPRIL/CN
L28             1 SEA ABB=ON  PLU=ON  FOSINOPRILAT/CN
L29             1 SEA ABB=ON  PLU=ON  IMIDAPRIL/CN
L30             1 SEA ABB=ON  PLU=ON  LISINOPRIL/CN
L31             1 SEA ABB=ON  PLU=ON  MOEXIPRIL/CN
L32             1 SEA ABB=ON  PLU=ON  PERINDOPRIL/CN
L33             1 SEA ABB=ON  PLU=ON  PERINDOPRILAT/CN
L34             1 SEA ABB=ON  PLU=ON  QUINAPRIL/CN
L35             1 SEA ABB=ON  PLU=ON  QUINAPRILAT/CN
L36             1 SEA ABB=ON  PLU=ON  RAMIPRIL/CN
L37             1 SEA ABB=ON  PLU=ON  SARALASIN ACETATE/CN
L38             1 SEA ABB=ON  PLU=ON  SPIRAPRIL/CN
L39             1 SEA ABB=ON  PLU=ON  TEMOCAPRIL/CN
L40             1 SEA ABB=ON  PLU=ON  TRANDOLAPRIL/CN
                E BIOPROJECT BP1.137/CN
                E CHIESI/CN
                E BP1.137/RN
                E BP1.137/CN
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                E BP1137/CN
                E BP1 137/CN
                E CHF 1514/CN
L41           1 SEA ABB=ON  PLU=ON  CHF 1514
                E FPL-66564/CN
                E FPL 66564/CN
L42           1 SEA ABB=ON  PLU=ON  FPL 66564/CN
L43           1 SEA ABB=ON  PLU=ON  IDRAPRIL/CN
                E MDL-100240/CN
                E MDL 100240/CN
L44           1 SEA ABB=ON  PLU=ON  MDL 100240/CN
                E S-5590/CN
                E S 5590/CN
L45           1 SEA ABB=ON  PLU=ON  S 5590/CN
L46          28 SEA ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR
                L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR
                L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR
                L42 OR L43 OR L44 OR L45)

     FILE 'HCAPLUS' ENTERED AT 16:45:27 ON 08 DEC 2005
L47          72 SEA ABB=ON  PLU=ON  L17 AND (L46 OR ANGIOTENSIN(S)?CONVERT?(S)(
                INHIB? OR BLOCK? OR ANTAG?) OR LOTENSIN OR CAPOTEN OR VASOTEC
                OR MONOPRIL OR PRINIVIL OR ZESTRIL OR UNIVASC OR ACCUPRIL OR
                ACEON OR ALTACE OR MAVIK OR ACE INHIB?)
L48           1 SEA ABB=ON  PLU=ON  L47 AND L1
                D KWIC L47 10
L49          64 SEA ABB=ON  PLU=ON  L47 AND THU/RL
L50           8 SEA ABB=ON  PLU=ON  L47 NOT L49

     FILE 'MEDLINE' ENTERED AT 16:51:22 ON 08 DEC 2005

     FILE 'REGISTRY' ENTERED AT 16:51:37 ON 08 DEC 2005
                SET SMARTSELECT ON
L51             SEL PLU=ON  L46 1- CHEM :     183 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE' ENTERED AT 16:51:40 ON 08 DEC 2005
L52       21896 SEA ABB=ON  PLU=ON  L51
L53       21896 SEA ABB=ON  PLU=ON  L46 OR L52
                D SCA
                D TRIAL
                E ANGIOTENSI CONVERT/CT
                E ANGIOTENSIN CONVERT/CT
                E E6+ALL
                E E2+ALL
L54       29253 SEA ABB=ON  PLU=ON  "ANGIOTENSIN-CONVERTING ENZYME INHIBITORS"+
                PFT,NT/CT
L55       32469 SEA ABB=ON  PLU=ON  L54 OR L53
L56       72785 SEA ABB=ON  PLU=ON  INFLAMMATORY BOWEL OR SHORT BOWEL OR
                "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR
                ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR
                POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA
L57          18 SEA ABB=ON  PLU=ON  L55 AND L56

     FILE 'EMBASE' ENTERED AT 16:54:39 ON 08 DEC 2005

     FILE 'REGISTRY' ENTERED AT 16:54:45 ON 08 DEC 2005
                SET SMARTSELECT ON
L58             SEL PLU=ON  L46 1- CHEM :     183 TERMS
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             SET SMARTSELECT OFF

     FILE 'EMBASE' ENTERED AT 16:54:46 ON 08 DEC 2005
L59        43028 SEA ABB=ON  PLU=ON  L58
L60        43028 SEA ABB=ON  PLU=ON  L46 OR L59
                 E ANGIOTENSIN CONVERT/CT
                 E E23+ALL
                 E E2+ALL
L61        65974 SEA ABB=ON  PLU=ON  DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+PFT,N
                 T,NXT/CT
L62        66865 SEA ABB=ON  PLU=ON  L60 OR L61
L63        57400 SEA ABB=ON  PLU=ON  INFLAMMATORY BOWEL OR SHORT BOWEL OR
                 "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR
                 ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR
                 POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA
L64          138 SEA ABB=ON  PLU=ON  L62 AND L63
                 D KWIC
L65           23 SEA ABB=ON  PLU=ON  L64 AND ANGIOTENSIN?


     FILE HOME

     FILE HCAPLUS

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     FILE COVERS 1907 - 8 Dec 2005  VOL 143 ISS 24
     FILE LAST UPDATED: 7 Dec 2005  (20051207/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

      This file contains CAS Registry Numbers for easy and accurate
      substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    7 DEC 2005  HIGHEST RN 869534-51-0
     DICTIONARY FILE UPDATES:   7 DEC 2005  HIGHEST RN 869534-51-0

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
```

```
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE
 FILE LAST UPDATED: 6 DEC 2005 (20051206/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

FILE EMBASE
 FILE COVERS 1974 TO 1 Dec 2005 (20051201/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
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=> fil hcap
FILE 'HCAPLUS' ENTERED AT 17:02:32 ON 08 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 8 Dec 2005 VOL 143 ISS 24
FILE LAST UPDATED: 7 Dec 2005 (20051207/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat l47

L4	7752	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) INFLAMMATORY"+PFT/CT
L5	261	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) SHORT BOWEL SYNDROME"+PFT/CT
L6	4	SEA FILE=HCAPLUS ABB=ON PLU=ON "INFLAMMATION (L) CROHN'S DISEASE"+PFT/CT
L7	4	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) CROHN'S"+PFT/CT
L8	2349	SEA FILE=HCAPLUS ABB=ON PLU=ON CELIAC DISEASE+PFT/CT
L9	4545	SEA FILE=HCAPLUS ABB=ON PLU=ON "INFLAMMATION (L) ULCERATIVE COLITIS"+PFT/CT
L10	4544	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) ULCERATIVE COLITIS"+PFT/CT
L11	2302	SEA FILE=HCAPLUS ABB=ON PLU=ON "STOMACH, DISEASE (L) ULCER"+PFT/CT
L12	130	SEA FILE=HCAPLUS ABB=ON PLU=ON "INFLAMMATION (L) DIVERTICULITIS"+PFT/CT
L13	130	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) DIVERTICULITIS"+PFT/CT
L14	199	SEA FILE=HCAPLUS ABB=ON PLU=ON "INFLAMMATION (L) RECTAL"+PFT/CT
L15	177	SEA FILE=HCAPLUS ABB=ON PLU=ON "INTESTINE, DISEASE (L) RECTUM, INFLAMMATION"+PFT/CT
L16	78	SEA FILE=HCAPLUS ABB=ON PLU=ON DIARRHEA+PFT/CT(L)CHRONIC
L17	21694	SEA FILE=HCAPLUS ABB=ON PLU=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR INFLAMMATORY BOWEL OR SHORT BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA
L18	1	SEA FILE=REGISTRY ABB=ON PLU=ON ALACEPRIL/CN
L19	1	SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL/CN
L20	1	SEA FILE=REGISTRY ABB=ON PLU=ON LOTENSIN/CN
L21	1	SEA FILE=REGISTRY ABB=ON PLU=ON CAPTOPRIL/CN
L22	1	SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL/CN
L23	1	SEA FILE=REGISTRY ABB=ON PLU=ON CERANAPRIL
L24	1	SEA FILE=REGISTRY ABB=ON PLU=ON DELAPRIL/CN
L25	1	SEA FILE=REGISTRY ABB=ON PLU=ON ENALAPRIL/CN
L26	1	SEA FILE=REGISTRY ABB=ON PLU=ON ENALAPRILAT/CN
L27	1	SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL/CN
L28	1	SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRILAT/CN
L29	1	SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL/CN
L30	1	SEA FILE=REGISTRY ABB=ON PLU=ON LISINOPRIL/CN
L31	1	SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL/CN
L32	1	SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL/CN
L33	1	SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRILAT/CN
L34	1	SEA FILE=REGISTRY ABB=ON PLU=ON QUINAPRIL/CN
L35	1	SEA FILE=REGISTRY ABB=ON PLU=ON QUINAPRILAT/CN
L36	1	SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL/CN

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L37             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SARALASIN ACETATE/CN
L38             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SPIRAPRIL/CN
L39             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TEMOCAPRIL/CN
L40             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRANDOLAPRIL/CN
L41             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CHF 1514
L42             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FPL 66564/CN
L43             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  IDRAPRIL/CN
L44             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MDL 100240/CN
L45             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  S 5590/CN
L46            28 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21 OR
                  L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR
                  L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR
                  L40 OR L41 OR L42 OR L43 OR L44 OR L45)
L47            72 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND (L46 OR ANGIOTENSIN(S)
                  ?CONVERT?(S)(INHIB? OR BLOCK? OR ANTAG?) OR LOTENSIN OR
                  CAPOTEN OR VASOTEC OR MONOPRIL OR PRINIVIL OR ZESTRIL OR
                  UNIVASC OR ACCUPRIL OR ACEON OR ALTACE OR MAVIK OR ACE INHIB?)


=> fil medline
FILE 'MEDLINE' ENTERED AT 17:02:40 ON 08 DEC 2005

 FILE LAST UPDATED: 6 DEC 2005 (20051206/UP). FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available. For details enter HELP
 RLOAD at an arrow promt (=>). See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que stat l57
L18             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALACEPRIL/CN
L19             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  BENAZEPRIL/CN
L20             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LOTENSIN/CN
L21             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CAPTOPRIL/CN
L22             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CILAZAPRIL/CN
L23             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CERANAPRIL
L24             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DELAPRIL/CN
L25             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENALAPRIL/CN
L26             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENALAPRILAT/CN
L27             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FOSINOPRIL/CN
L28             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FOSINOPRILAT/CN
L29             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  IMIDAPRIL/CN
L30             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LISINOPRIL/CN
L31             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MOEXIPRIL/CN
L32             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PERINDOPRIL/CN
L33             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PERINDOPRILAT/CN
L34             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  QUINAPRIL/CN
L35             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  QUINAPRILAT/CN
```

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L36             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  RAMIPRIL/CN
L37             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SARALASIN ACETATE/CN
L38             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SPIRAPRIL/CN
L39             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TEMOCAPRIL/CN
L40             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRANDOLAPRIL/CN
L41             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CHF 1514
L42             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FPL 66564/CN
L43             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  IDRAPRIL/CN
L44             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MDL 100240/CN
L45             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  S 5590/CN
L46            28 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21 OR
                  L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR
                  L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR
                  L40 OR L41 OR L42 OR L43 OR L44 OR L45)
L51               SEL  PLU=ON  L46 1- CHEM :     183 TERMS
L52         21896 SEA FILE=MEDLINE ABB=ON  PLU=ON  L51
L53         21896 SEA FILE=MEDLINE ABB=ON  PLU=ON  L46 OR L52
L54         29253 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANGIOTENSIN-CONVERTING
                  ENZYME INHIBITORS"+PFT,NT/CT
L55         32469 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 OR L53
L56         72785 SEA FILE=MEDLINE ABB=ON  PLU=ON  INFLAMMATORY BOWEL OR SHORT
                  BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS?
                  OR ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR
                  POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA
L57            18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L55 AND L56


=> fil embase
FILE 'EMBASE' ENTERED AT 17:02:48 ON 08 DEC 2005
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 FILE COVERS 1974 TO 1 Dec 2005 (20051201/ED)

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=> d que stat l65
L18             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALACEPRIL/CN
L19             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  BENAZEPRIL/CN
L20             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LOTENSIN/CN
L21             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CAPTOPRIL/CN
L22             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CILAZAPRIL/CN
L23             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CERANAPRIL
L24             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DELAPRIL/CN
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L26             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENALAPRILAT/CN
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L62         66865 SEA FILE=EMBASE ABB=ON  PLU=ON  L60 OR L61
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                  OR ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR
                  POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA
L64           138 SEA FILE=EMBASE ABB=ON  PLU=ON  L62 AND L63
L65            23 SEA FILE=EMBASE ABB=ON  PLU=ON  L64 AND ANGIOTENSIN?


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FILE 'HCAPLUS' ENTERED AT 17:02:59 ON 08 DEC 2005
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FILE 'MEDLINE' ENTERED AT 17:02:59 ON 08 DEC 2005

FILE 'EMBASE' ENTERED AT 17:02:59 ON 08 DEC 2005
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PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L57
PROCESSING COMPLETED FOR L65
L66           103 DUP REM L47 L57 L65 (10 DUPLICATES REMOVED)
                  ANSWERS '1-72' FROM FILE HCAPLUS
                  ANSWERS '73-86' FROM FILE MEDLINE
                  ANSWERS '87-103' FROM FILE EMBASE

=> s l66 and py<2005
L67            72 L66 AND PY<2005

=> d l67 ibib abs hitind 1-72

L67  ANSWER 1 OF 72  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1223666  HCAPLUS
TITLE:                    Drug discovery assays based on the biology of chronic
                          disease
INVENTOR(S):              Polansky, Hanan
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 307 pp., Cont.-in-part of U.S.
                          Ser. No. 223,050.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
```

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005255458	A1	20051117	US 2003-611217	20030701
US 2003068616	A1	20030410	US 2002-223050	20020814 <--
PRIORITY APPLN. INFO.:			US 2002-223050	A2 20020814
			US 2000-732360	A2 20001207

AB Using the recently discovered biol. of chronic disease, the invention presents new methods for evaluating the effectiveness of a compound for use in modulating the progression of chronic disease, for determining whether a subject has a chronic disease, or has an increased risk of developing clin. symptoms associated with such disease, and for treating chronic disease.

IC ICM C12Q001-70
ICS C12Q001-68
INCL 435005000; 435006000
CC 1-1 (Pharmacology)
Section cross-reference(s): 14
IT INDEXING IN PROGRESS
IT **Intestine, disease**
(**inflammatory**; drug discovery assays based on biol. of chronic disease)
IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)- 50-78-2, Aspirin 51-41-2, Norepinephrine 58-22-0, Testosterone 66-81-9, Cycloheximide 156-54-7, Sodium butyrate 302-79-4, all-trans-Retinoic acid 362-74-3, Dibutyryl cyclic amp 521-18-6, Dihydrotestosterone 965-93-5, R1881 7481-89-2, DdC 7683-59-2, Isoprenaline 9002-68-0, FSH 11128-99-7, Angiotensin II 13721-39-6, Sodium orthovanadate 16561-29-8, TPA (phorbol derivative) 30516-87-1, Azt 56092-81-0, Ionomycin 56180-94-0, Acarbose **62571-86-2**, Captopril 66575-29-9, Forskolin 69655-05-6, DdI 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81872-10-8, Zofenopril **87333-19-5**, Ramipril
RL: PAC (Pharmacological activity); BIOL (Biological study)
(drug discovery assays based on biol. of chronic disease)

L67 ANSWER 2 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:122803 HCAPLUS
DOCUMENT NUMBER: 142:219083
TITLE: Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents
INVENTOR(S): Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan; Berstein, David L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 635,054.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005032825	A1	20050210	US 2004-862149	20040604
US 2003220297	A1	20031127	US 2003-357152	20030203 <--

US 2004073024 A1 20040415 US 2003-635054 20030806 <--
PRIORITY APPLN. INFO.: US 2002-353252P P 20020201
US 2002-426928P P 20021115
US 2002-428383P P 20021122
US 2002-438930P P 20021217
US 2003-357152 A2 20030203
US 2003-635054 A2 20030806
OTHER SOURCE(S): MARPAT 142:219083
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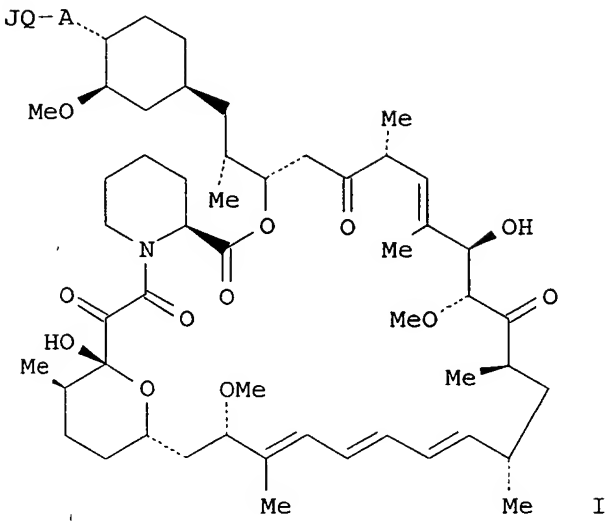


I

AB Rapamycin derivs. containing phosphorus moiety, such as I [A = O, S, NR2, absent; Q = V, OV, SV, NR2, absent; V = aliphatic, heteroaliph., aryl, heteroaryl moiety, such that J is linked to the cyclohexyl ring directly, through A or through VA, OVA, SVA or NR2VA; J = P(:K)(YR5)2, P(YR5)2, P(:K)(YR5)GR6; K = O, S; Y = O, S, NR2, bond; R2, R5 = aliphatic, heteroaliph., aryl, heteroaryl, H; R6 = PK(YR5)YR5, SO2YR5, C(O)YR5; G = O, S, NR2, (M)X; M = (un)substituted methylene, alkyl, alkylene; X = 1-6], and pharmaceutically acceptable derivs. thereof, were prepared for therapeutic use as immunosuppressive and anticancer agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, **inflammatory bowel** disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-QJ = OP(O)(OBu)Me] was prepared by reacting rapamycin with methylphosphonic dichloride and n-butanol using 3,5-lutidine in CH2Cl2 under a nitrogen atmospheric Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IC ICM A61K031-675
ICS A61K031-4745

INCL 514291000; 540456000; 514080000
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63
IT **Intestine, disease**
(**inflammatory**; preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)
IT 50-07-7, Mitomycin C 50-28-2, Estradiol, biological studies 51-21-8, 5-Fluorouracil 51-43-4D, Epinephrine, cisplatin gel 52-53-9, Verapamil 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-05-9, Leucovorin 59-05-2, Methotrexate 81-81-2, Warfarin 127-07-1, Hydroxyurea 147-94-4D, Cytarabine, liposomal 148-82-3, Melphalan 154-93-8D, Gliadel, Wafer 298-81-7, Methoxsalen 302-79-4, Tretinoin 305-03-3, Chlorambucil 315-30-0, Zyloprim 525-66-6, Propranolol 637-07-0, Clofibrate 645-05-6, Altretamine 943-45-3D, Fibric acid, derivs. 1327-53-3, Arsenic trioxide 2998-57-4, Estramustine 3778-73-2, Ifosfamide 3930-20-9, Sotalol 4291-63-8, Cladribine 7280-37-7, Estropipate 9005-49-6, Heparin, biological studies 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 14769-73-4, Levamisol 14807-96-6, Talc, biological studies 15663-27-1, Cisplatin 19767-45-4, Mesna 20537-88-6, Amifostine 20830-81-3, Daunorubicin 20830-81-3D, Daunorubicin, liposomal 21679-14-1, Fludarabine 21829-25-4, Nifedipine 23214-92-8, Doxorubicin 24584-09-6, Dexrazoxane 25812-30-0, Gemfibrozil 26839-75-8, Timolol 29122-68-7, Atenolol 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 37517-30-9, Acebutolol 38363-40-5, Penbutolol 40391-99-9, Pamidronate 41575-94-4, Carboplatin 42200-33-9, Nadolol 42399-41-7, Diltiazem 51384-51-1, Metoprolol 51781-06-7, Carteolol 53910-25-1, Pentostatin 55985-32-5, Nicardipine 56124-62-0, Valrubicin 56420-45-2, Epirubicin 57852-57-0, Idamycin 58957-92-9, Idarubicin **62571-86-2**, Captopril 63659-18-7, Betaxolol 63675-72-9, Nisoldipine 64706-54-3, Bepridil 65271-80-9, Mitoxantrone 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 71486-22-1, Vinorelbine 72509-76-3, Felodipine 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81147-92-4, Esmolol **82834-16-0**, Perindopril **85441-61-8**, Quinapril 85622-93-1, Temozolomide **87333-19-5**, Ramipril **87679-37-6**, Trandolapril 87806-31-3, Porfimer sodium 88150-42-9, Amlodipine 89778-26-7, Toremifene 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 97682-44-5, Irinotecan **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 107868-30-4, Exemestane 112809-51-5, Letrozole 114798-26-4, Losartan 114977-28-5, Docetaxel 117091-64-2, Etoposide phosphate 118072-93-8, Zoledronate 123948-87-8, Topotecan 129453-61-8, Fulvestrant 134523-00-5, Atorvastatin 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145781-92-6, Goserelin acetate 153559-49-0, Bexarotene 154361-50-9, Capecitabine 169590-42-5, Celecoxib 174722-31-7, Rituximab 180288-69-1, Trastuzumab 216503-57-0, Alemtuzumab 216974-75-3, Avastin 220127-57-1, Imatinib mesylate 220578-59-6, Gemtuzumabozogamicin 346689-77-8, XR11576 387867-13-2, MLN518 391208-93-8, Glycogen synthase kinase 3 612092-74-7, MLN 591 679809-58-6, Enoxaparin 811442-46-3, MLN 2704
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)

L67 ANSWER 3 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:78296 HCAPLUS
DOCUMENT NUMBER: 142:170088
TITLE: Methods for the treatment of gastrointestinal disorders using guanylate cyclase C receptor activators, such as ST peptide variants
INVENTOR(S): Currie, Mark G.; Mahajan-Miklos, Shalina
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 766,735.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020811	A1	20050127	US 2004-796719	20040309
US 2004266989	A1	20041230	US 2004-766735	20040128 <--
WO 2005087797	A1	20050922	WO 2005-US7752	20050308

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-443098P	P	20030128
US 2003-471288P	P	20030515
US 2003-519460P	P	20031112
US 2004-766735	A2	20040128
US 2004-796719	A	20040309
US 2004-845895	A	20040514
US 2004-899806	A	20040727
US 2005-54071	A	20050208

OTHER SOURCE(S): MARPAT 142:170088

AB The present invention features compns. and related methods for treating irritable bowel syndrome (IBS) and other gastrointestinal disorders and conditions using peptides and other agents that activate the guanylate cyclase C (GC-C) receptor. The gastrointestinal disorders include gastrointestinal motility disorders, functional gastrointestinal disorders, gastro-esophageal reflux disease (GERD), Crohn's disease, **ulcerative colitis, inflammatory bowel** disease, functional heartburn, dyspepsia (including functional dyspepsia or nonulcer dyspepsia), gastro-paresis, chronic intestinal pseudo-obstruction (or colonic pseudo-obstruction), and disorders and conditions associated with constipation, e.g., constipation associated with use of opiate pain killers, post-surgical constipation, and constipation associated with neuropathic disorders as well as other conditions and disorders. Provided are sequences of the peptides of the invention , as well as a method for there preparation The peptides of the invention, like the bacterial ST peptides, have six Cys residues. These six Cys residues form three disulfide bonds in the mature and active form of the peptide. If the six Cys residues are identified, from the amino to carboxy terminus of the peptide, as A, B, C, D, E, and F, then the disulfide bonds form as

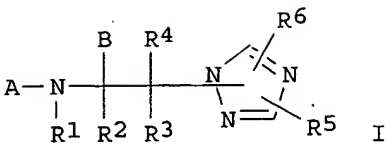
follows: A-D, B-E, and C-F. The formation of these bonds is thought to be important for GC-C receptor binding. Certain of the peptides of the invention include a potentially functional chymotrypsin cleavage site. Cleavage at chymotrypsin cleavage site reduces or eliminates the ability of the peptide to bind to the GC-C receptor. It is expected that chymotrypsin cleavage will moderate the action of a peptide of the invention having an appropriately positioned chymotrypsin cleavage site as the peptide passes through the intestinal tract.

IC ICM C07K007-08
ICS C07K007-06
INCL 530327000; 530328000
CC 1-9 (Pharmacology)
IT **Intestine, disease**
(**inflammatory**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)
IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)
IT 9015-82-1, **Angiotensin-converting** enzyme 9068-52-4, CGMP Phosphodiesterase 37255-34-8, 5α-Reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)

L67 ANSWER 4 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1127349 HCAPLUS
DOCUMENT NUMBER: 142:74574
TITLE: Preparation of 1,2,4-triazolylethylamines as modulators of the glucocorticoid receptor
INVENTOR(S): Robinson, Leslie; Rueter, Jaimie K.; Moree, Wilna J.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111015	A1	20041223	WO 2004-US18487	20040611 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004266831	A1	20041230	US 2004-865443	20040610 <--
PRIORITY APPLN. INFO.:			US 2003-477545P	P 20030611
OTHER SOURCE(S):	MARPAT 142:74574			

GI



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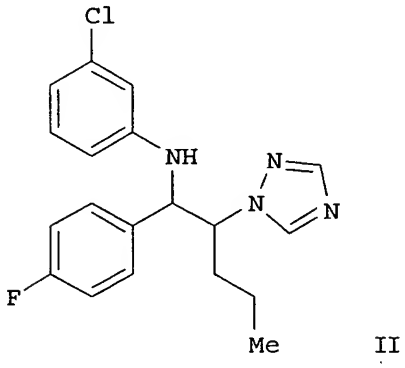


II

AB Title compds. I [A, B = cycloalkyl, aryl, heteroaryl; R1 = H, acyl, carboxy, etc.; R2-4 = H, alkyl, heteroalkyl, etc.; R5-6 = H, F, Cl, Br, etc.] are prepared General synthetic procedures are provided for the synthesis of 19 examples, e.g., II. Example compds. are tested in a glucocorticoid receptor binding assay in the range of 0.1 nM to 40 μM [no data]. I are glucocorticoid receptor modulators and are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes, inflammatory and immune disorders.

IC ICM C07D249-08

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Intestine, disease**
(**inflammatory**; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-78-2, Aspirin 51-21-8, 5-Fluorouracil 51-64-9, Dexamphetamine 52-24-4, Thiotepa 52-53-9, Verapamil 53-03-2, Prednisone 53-86-1, Indomethacin 56-03-1, Biguanide 58-32-2, Dipyridamole 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 67-78-7, Triamcinolone diacetate 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 5536-17-4, Vidarabine 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15687-27-1, Ibuprofen 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 36322-90-4,

Piroxicam 41575-94-4, Carboplatin 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 59277-89-3, Aciclovir **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 82410-32-0, Ganciclovir **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 104987-11-3, FK-506 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 136470-78-5, Abacavir 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Rofecoxib 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS30440 169590-42-5, Celecoxib 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98 282526-98-1 335149-08-1, L 895645 335149-14-9, R 119702 335149-15-0, KAD 1129 335149-17-2, ARHO 39242 335149-19-4 335149-23-0, NVP-DPP 728A 335149-25-2, CP 331648 430433-17-3, Glipyride
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

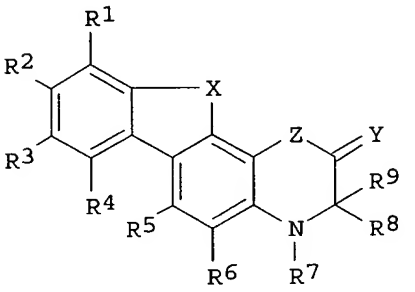
IT 9001-62-1, Lipase 9015-82-1, **ACE** 9027-63-8 9028-35-7 9033-06-1, Glucosidase 9077-14-9, Squalene synthetase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitor**, combination pharmaceutical; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1124594 HCAPLUS
DOCUMENT NUMBER: 142:79882
TITLE: Non-steroidal compound modulators of the glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist dependent diseases
INVENTOR(S): Hadida-Ruah, Sara Sabine; He, Xiaohui; Nagasawa, Johnny Yasuo
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004110385 A2 20041223 WO 2004-US18677 20040611 <--
WO 2004110385 A3 20050127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004266758 A1 20041230 US 2004-865444 20040610 <--
PRIORITY APPLN. INFO.: US 2003-477574P P 20030611
OTHER SOURCE(S): MARPAT 142:79882
GI



I

AB The present invention relates to new non-steroidal compds. which are glucocorticoid receptor (GR) modulators (that is agonists and antagonists) and thus are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes and inflammatory or immune associated diseases, and to a method for using such compds. to treat these and related diseases. Specifically, the novel non-steroidal compds. have the structure as formula (I), wherein R1 through R6 are independently (i) hydrogen, F, C1, Br, I, NO2, CN, or OR10, etc, (ii) C1-6-alkyl, C3-8-cycloalkyl, or C2-6-alkenyl, etc; R7 is hydrogen, C1-6-alkyl, or C3-8-cycloalkyl, etc; R8 and R9 are independently hydrogen, C1-6-alkyl, or C3-8-cycloalkyl, etc; Y is O, S, or NR14; Z is O, S, S(O), S(O)2, or NR15; and X is OCR16R17, SCR16R17, S(O)CR16R17, etc.

IC ICM A61K
CC 63-5 (Pharmaceuticals)
IT **Intestine, disease**
(**inflammatory**; non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist-dependent diseases)
IT 5-HT reuptake inhibitors
Addison's disease
Allergy
Anti-inflammatory agents
Antibiotics
Antidepressants
Antidiabetic agents
Antihypertensives
Antiobesity agents

Antitumor agents
Antiviral agents
Appetite depressants
Arteriosclerosis
Asthma
Atherosclerosis
Autoimmune disease
Behcet's syndrome
Blood, disease
Calcium channel blockers
Celiac disease
Connective tissue, disease
Dermatomyositis
Digestive tract, disease
Eczema
Endocrine system, disease
Eye, disease
Fungicides
Graves' disease
Hay fever
Hepatitis
Hypolipemic agents
Immunosuppressants
Leukemia
Lymphoma
Multiple sclerosis
Myasthenia gravis
Obesity
Platelet aggregation inhibitors
Psoriasis
Rheumatic diseases
Rheumatoid arthritis
Seborrhea
Sepsis
Sjogren's syndrome
Transplant rejection
Urticaria
(non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist-dependent diseases)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist-dependent diseases)

IT 9001-62-1, Lipase 9015-82-1, **Angiotensin-converting** enzyme 9027-63-8, ACAT 9029-60-1, Lipoxygenase 82707-54-8, Neutral endopeptidase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitor**; non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or **antagonist**-dependent diseases)

IT 50-18-0, Cyclophosphamide 50-78-2, Aspirin 51-21-8, 5-Fluorouracil 51-64-9, Dexamphetamine 52-24-4, Thiotepa 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 446-86-6 483-60-3 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivative 4205-91-8 7772-99-8, Tin II chloride, biological studies 10238-21-8,

Glyburide 14838-15-4, Phenylpropanolamine 15663-27-1, Cisplatin 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 41575-94-4, Carboplatin 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 89149-10-0, Deoxyspergualin 89750-14-1, Glucagon-like peptide-1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 104987-11-3, FK 506 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 144288-97-1, TS 962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, NN 2344 199914-96-0, YM 440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P 32/98 282526-98-1 287714-41-4 335149-08-1, L 895645 335149-14-9, R 119702 335149-15-0, KAD 1129 335149-17-2, ARHO 39242 335149-19-4 335149-23-0, NVP-DPP 728A 335149-25-2, CP 331648 430433-17-3, Glipyride 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist-dependent diseases)

L67 ANSWER 6 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:1124587 HCAPLUS
DOCUMENT NUMBER:	142:69188
TITLE:	Combination therapy for the treatment of diabetes
INVENTOR(S):	Erondu, Ngozi E.; Fong, Tung M.; MacNeil, Douglas J.; Van Der Ploeg, Leonardus H. T.; Kanatani, Akio
PATENT ASSIGNEE(S):	Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SOURCE:	PCT Int. Appl., 109 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110375	A2	20041223	WO 2004-US17291	20040602 <--
WO 2004110375	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-476388P P 20030606

OTHER SOURCE(S): MARPAT 142:69188

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-diabetic agent useful for the treatment of diabetes, diabetes associated with obesity and diabetes-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IC ICM A61K

CC 1-10 (Pharmacology)
Section cross-reference(s): 2

IT **Intestine, disease**
(**inflammatory**; combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

IT 51-64-9, Dextroamphetamine 52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 58-94-6D, Thiazide, derivs. 59-67-6, Niacin, biological studies 77-36-1, Chlorthalidone 83-46-5, β-Sitosterol 86-54-4, Hydralazine 90-84-6, Diethylpropion 100-55-0, Nicotinyl alcohol 120-97-8, Dichlorophenamide 122-09-8, Phentermine 134-49-6, Phenmetrazine 135-09-1, Hydroflumethiazide 156-08-1, Benzphetamine 156-34-3, Levamfetamine 300-62-9, Amphetamine 396-01-0, Triamterene 434-43-5, Pentorex 457-87-4, N-Ethylamphetamine 458-24-2, Fenfluramine 461-78-9, Chlorphentermine 525-66-6, Propranolol 532-52-5, Cyclexedrine 537-46-2, Methamphetamine 634-03-7, Phendimetrazine 637-07-0, Clofibrate 720-76-3, Fluminorex 943-45-3D, Fibric acid, derivs. 2207-50-3, Aminorex 2609-46-3, Amiloride 3239-44-9, Dexfenfluramine 3876-10-6, Clominorex 3930-20-9, Sotalol 4205-90-7, Clonidine 4378-36-3, Fenbutrazate 5051-62-7, Guanabenz 8075-95-4, Atromid 9004-10-8, Insulin, biological studies 9004-54-0D, Dextran, crosslinked, dialkylaminoalkyl derivs., biological studies 9028-35-7, HMG-CoA reductase 10238-21-8, Glyburide 10389-73-8, Clortermine 11041-12-6, Cholestyramine 13364-32-4, Clobenzorex 13445-60-8, Furfurylmethylamphetamine 13523-86-9, Pindolol 13862-07-2, Diphemethoxidine 14261-75-7, Cloforex 14838-15-4, Phenylpropanolamine 15221-81-5, Fludorex 15351-09-4, Metamfepramone 16397-28-7, Fenproporex 16662-47-8, Gallopamil 17243-57-1, Mefenorex 19216-56-9, Prazosin 21829-25-4, Nifedipine 22232-71-9, Mazindol 23288-49-5, Probucol 24558-01-8, Levophacetoperane 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 26844-12-2, Indoramin 28395-03-1, Bumetanide 29122-68-7, Atenolol 31036-80-3, Lofexidine 31428-61-2, Tiamenidine 31637-97-5, Etofibrate 34661-75-1, Urapidil 34887-52-0, Fenisorex 35795-16-5, Trimazosin 36393-56-3, Norpseudoephedrine 37296-80-3, Colestid 37517-30-9, Acebutolol 38304-91-5, Minoxidil 38363-40-5, Penbutolol 39562-70-4, Nitrendipine

41859-67-0 42017-89-0, Fenofibric acid 42200-33-9, Nadolol
42399-41-7, Diltiazem 49562-28-9, Tricor 50925-79-6, Colestipol
51384-51-1, Metoprolol 51781-06-7, Carteolol 52214-84-3, Ciprofibrate
54187-04-1, Rilmenidine 54870-28-9D, Meglitinide, derivs. 55121-56-7D,
Azetidinone, derivs. 55985-32-5, Nicardipine 56211-40-6, Torasemide
56980-93-9, Celiprolol 57149-07-2, Naftopidil 59170-23-9, Bevantolol
60607-68-3, Indenolol 62510-56-9, Picilorex **62571-86-2**,
Captopril 62658-63-3, Bopindolol 63590-64-7, Terazosin 63659-18-7,
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Nimodipine 66722-44-9, Bisoprolol 68291-97-4, Zonisamide 68377-92-4,
Arotinolol 71548-66-8, Beclofibrate 72509-76-3, Felodipine
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103890-78-4, Lacidipine 104713-75-9, Barnidipine 105979-17-7,
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111902-57-9, Temocapril 112573-73-6, Ecadotril 114798-26-4,
Losartan 118457-14-0, Nebivolol 122320-73-4, Rosiglitazone
123122-55-4, Candoxatril 123524-52-7, Azelnidipine 129981-36-8,
Sampatrilat 132203-70-4 133040-01-4, Eprosartan 134523-00-5,
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Pratosartan 163222-33-1, Ezetimibe 166518-60-1, Avasimibe
167221-71-8, Clevidipine 167305-00-2, Omapatrilat 169494-85-3, Leptin
169494-85-3D, Leptin, derivs. 180384-57-0, Tezosentan 182815-43-6,
Colesevelam 183293-82-5, Gemcabene 186390-48-7, CP346086
202340-45-2, Eflucimibe 211513-37-0, JTT 705 221564-97-2, BM 170744
256397-11-2, LAB 687 256532-03-3, WHIP 164 262352-17-0, Torcetrapib
265129-71-3, GW 7647 278779-30-9, GW 4064 289037-67-8, SC435
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532632 812697-41-9, BAY 63-2149 812697-42-0, SC 591 812697-56-6, SR
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BARI 1453 812697-67-9, PHA 384640 812697-68-0, AZD 7706 812697-87-3,
ER 4030 812697-90-8, A 308165 812697-92-0, YM 62899 812697-93-1, EXP
3137 812697-94-2, F 16828K 812697-96-4, XEN 010
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combination therapy of diabetes and diabetes-related disorders using
antiobesity agent and antidiabetic agent and other agents)

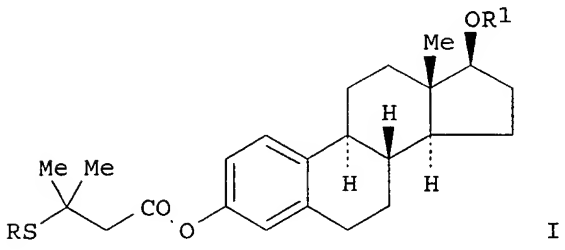
L67 ANSWER 7 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995933 HCAPLUS
DOCUMENT NUMBER: 141:424343
TITLE: Preparation of nitrosated and nitrosylated compounds for use in pharmaceutical compositions a nitric oxide (NO) donors
INVENTOR(S): Earl, Richard A.; Garvey, David S.; Gaston, Ricky D.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Stevenson, Cheri A.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098538	A2	20041118	WO 2004-US7943	20040315 <--
WO 2004098538	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-453963P P 20030313
US 2003-482134P P 20030625

OTHER SOURCE(S): MARPAT 141:424343
GI



I

AB Nitroso and nitrosyl derivs. of therapeutic agents, such as R-SNO, R-ONO, R-ONO2 [R = antithrombogenic agent, thrombolytic agent, fibrinolytic agent, vasospasm **inhibitor**, potassium channel **blocker**, calcium channel **blocker**, antihypertensive agent, antimicrobial agent, antibiotic, platelet reducing agent, antimitotic agent, antiproliferative agent, microtubule **inhibitor**, antisecretory agent, remodeling **inhibitor**, antisense nucleotide, anticancer chemotherapeutic agent, steroid, nonsteroidal antiinflammatory agent, selective COX-2 **inhibitor**, immunosuppressive agent, growth

factor **antagonist** or antibody, dopamine agonist, radiotherapeutic agent, heavy metal functioning as a radioplaque agent, biol. agent, aldosterone **antagonist**, α-adrenergic receptor **antagonist**, **angiotensin** II **antagonist**, β-adrenergic agonist, antihyperlipidemic drug, **angiotensin converting** enzyme (**ACE**) **inhibitor**, antioxidant, β-adrenergic **antagonist**, endothelin **antagonist**, neutral endopeptidase **inhibitor**, renin **inhibitor**, free radical scavenger, iron chelator, sex hormone, antipolymerase, antiviral agent, photodynamic therapy agent, antibody targeted therapy agent, gene therapy agent, etc.], were prepared for therapeutic use. The compds. and compns. of this invention can also be bound to a matrix. These nitroso- and nitro-compds. are claimed for use in treating cardiovascular diseases, for inhibiting platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation; transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative or vascular diseases; for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis by administering at least one compound of the invention that is optionally nitrosated and/or nitrosylated, in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions. The compds. of this invention are preferably estradiol compds., troglitazone compds., tranilast compds., retinoic acid compds., resveratrol compds., mycophenolic acid compds., acid compds., anthracenone compds. and trapidil compds. The cardiovascular diseases for treatment include restenosis, coronary artery disease, atherosclerosis, atherogenesis, cerebrovascular disease, angina, ischemic disease, congestive heart failure or pulmonary edema associated with acute myocardial infarction, aneurysm, thrombosis, hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, a vascular or non-vascular complication associated with the use of a medical device, wounds associated with the use of a medical device, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or a bleeding disorder. The autoimmune diseases for treatment include a pathol. condition resulting from abnormal cell proliferation, polycystic kidney disease, an inflammatory disease, for preserving an organ and/or a tissue or for inhibiting wound contraction in a patient. The pathol. conditions resulting from abnormal cell proliferation include is a cancer, a Karposi's sarcoma, a cholangiocarcinoma, a choriocarcinoma, a neoblastoma, a Wilm's tumor, Hodgkin's disease, a melanoma, multiple myelomas, a chronic lymphocytic leukemia or an acute or chronic granulocytic lymphoma. The inflammatory diseases for treatment includerheumatoid arthritis, an inflammatory skin disease, restenosis, multiple sclerosis, a surgical adhesion, tuberculosis, a graft rejection, an inflammatory lung disease, an **inflammatory bowel** disease, an inflammatory disease that affects or causes obstruction of a body passageway, an inflammation of the eye, an inflammation of the nose, an inflammation of the throat or a neovascular diseases of the eye. Thus, S-mono- and O,S-dinitroso-β-estradiol derivs. I (R = NO, R1 = H, NO) were prepared via an esterification reaction of β-estradiol with 3-methyl-3-(2,4,6-trimethoxyphenylmethylthio)butyric acid using EDAP and DMAP in DMF to form mono-ester I [R = CH2C6H2-2,4,6-(OMe)3, R1 = H], cleavage of the trimethoxybenzyl S-protecting group of the mono-ester using L-cysteine and TFA in CH2Cl2 to give thiol I (R = R1 = H), and finally, treatment of the thiol with Bu nitrite in CH2Cl2 to form the desired S-mono- and O,S-dinitroso-β-estradiol derivs. The prepared compds. were assayed

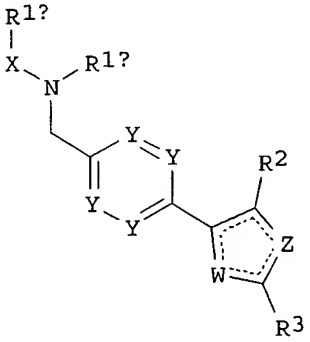
for suppression of proliferation of human coronary artery smooth muscle cells.
IC ICM A61K
CC 32-3 (Steroids)
Section cross-reference(s): 1, 25, 28, 30, 63

L67 ANSWER 8 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:817878 HCAPLUS
DOCUMENT NUMBER: 141:332038
TITLE: Bicyclic compounds, particularly N-[(butyloxy)carbonyl]-3-[4-[(substituted-amino)methyl]phenyl]-5-isobutylthiophene-2-sulfonamides, useful as angiotensin II (AT2 receptor) agonists, and their uses, pharmaceutical formulations, preparation, and intermediates
INVENTOR(S): Hallberg, Anders; Alterman, Mathias
PATENT ASSIGNEE(S): Vicore Pharma AB, Swed.; McNeeney, Stephen Phillip
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

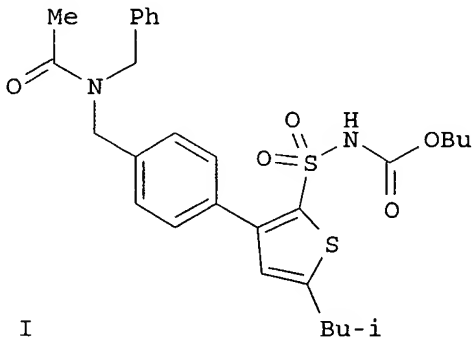
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085420	A1	20041007	WO 2003-GB1251	20030324 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-GB1251 20030324
OTHER SOURCE(S): MARPAT 141:332038
GI



I



II

AB Title compds. I and their pharmaceutically-acceptable salts are provided [wherein: X = O, CO, SO2; R1a, R1b = H, alkyl, alkoxyalkyl, Ar1, Het1,

alkyl-Het2, alkoxy-Ar3, alkoxy-Het3; or when X = CO then R1a may also be alkoxy or -O-Ar4; Ar1-Ar4 = (independently) (un)substituted C6-10 aryl; Het1-Het3 = (independently) (un)substituted 4- to 12-membered N/O/S heterocycle; Y = (independently) CH or CF; Z = CH, O, S, N, or CH:CH; W = CH, O, S, or N; R2 = SO2NHCOR4, SO2NHSO2R4, or CONHSO2R4; or when Z = CH:CH then also R2 = NHSO2NHCOR5 or NHCONHSO2R5; R3 = alkyl, alkoxy, or alkoxyalkyl; R4 = alkyl, alkoxy, alkoxyalkyl, or (di)alkylamino; R5 = alkyl; provided (1) that Z ≠ W, (2) that W = CH or N when Z = CH:CH, and (3) that, except when Z = CH:CH and W = CH, then if Z or W = CH, then the other = O or S]. I and salts are useful as selective agonists of the AT2 receptor. As such, they are useful for treatment of a wide variety of conditions, and thus, in particular, in the treatment of (inter alia) gastrointestinal conditions, such as dyspepsia, IBS and MOF, and cardiovascular disorders. Prepns. of 15 compds. I are described. For instance, amidation of thiophene-2-sulfonyl chloride with tert-butylamine, followed by lithiation with BuLi and alkylation with 1-iodo-2-methylpropane, gave 5-isobutyl-N-tert-butylthiophene-2-sulfonamide. This compound underwent a sequence of lithiation in the 3-position with BuLi, boronation with B(OPr-iso)3, and Pd(OAc)2/PPh3-catalyzed coupling with 4-bromobenzaldehyde, to give 3-(4-formylphenyl)-5-isobutyl-N-tert-butylthiophene-2-sulfonamide. This key aldehyde intermediate underwent reductive amination with various amines and NaBH4, followed by N-acylation with acid chlorides or alkyl chloroformates, deprotection of the sulfonamide with TFA and anisole, and N-acylation of the sulfonamide N with n-Bu chloroformate. Using PhCH2NH2 and AcCl in the last steps, example compound II was prepared The example compds. bound preferentially to porcine myometrial membrane AT2 receptors, showing Ki less than 50 nM, whereas they bound to rat liver membrane AT1 receptors with Ki = 1 μM or greater. In a duodenal mucosal alkaline secretion assay in anesthetized rats, the example compds. markedly stimulated mucosal alkalization (no data); this effect was blocked by coadministration of the selective AT2 receptor antagonist PD123319.

IC ICM C07D333-34
ICS C07D409-12; C07D333-38; A61K031-381; A61P009-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Intestine, disease**
(**inflammatory**, treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT Angiogenesis
Apoptosis
Asthma
Atherosclerosis
Autoimmune disease
Biliary tract, disease
Cardiovascular system, disease
Celiac disease
Central nervous system, disease
Cognitive disorders
Diarrhea
Digestive tract, disease
Dyspepsia
Eating disorders
Eye, disease
Gallbladder, disease
Hepatitis
Hypertension
Hypertrophy

Inflammation
Ischemia
Kidney, disease
Liver, disease
Multiple organ failure
Nausea
Neoplasm
Obesity
Preeclampsia
Psoriasis
Respiratory system, disease
Sepsis
Sjogren's syndrome
Thirst
Transplant rejection
Ulcer
Vomiting
(treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT **Stomach, disease**
(**ulcer**, treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**, treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT 9015-82-1, **Angiotensin converting** enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic compns. containing **inhibitors** of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as **angiotensin** II (AT2 receptor) agonists)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 9 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:817632 HCAPLUS
DOCUMENT NUMBER: 141:307605
TITLE: Pharmaceutical compositions using transition metal chelators for inhibiting metal ion-dependent enzymatic activity, and therapeutic use
INVENTOR(S): Appelbaum, Jerachmiel
PATENT ASSIGNEE(S): Israel
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004084799	A2	20041007	WO 2004-IL279	20040325 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IL 2003-155111 A 20030327

AB The invention provides pharmaceutical compns. for inhibiting pathol. functions of metal-dependent metalloproteases, as well as for neutralizing bacterial virulence factors, by employing chelators of transition metals, resulting in reduction in the availability of such metals, or by replacing the key metal ions with different ions. In addition, the invention discloses the use of such metalloprotease inhibitors for the manufacture of a pharmaceutical composition for the prevention or treatment of pathol. conditions influenced by the action of metalloproteases. The invention further discloses methods of treatment or prevention of such conditions.

IC ICM A61K

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; transition metal chelators for inhibiting metal ion-dependent enzymes, and therapeutic use)

IT 52-67-5, Penicillamine 107-15-3, Ethylenediamine, biological studies 111-40-0, Diethylenetriamine 111-41-1 112-24-3, Triethylenetetramine 112-57-2 280-57-9, Triethylenediamine 4067-16-7, Pentaethylenehexamine 7440-56-4, Germanium, biological studies 7440-56-4D, Germanium, compds. 7440-56-4D, Germanium, complexes with TPEN 16858-02-9D, Tpen, derivs. 16858-02-9D, TPEN, germanium complexes 21121-06-2, Triethylenetetramine hydrochloride 21121-07-3, Tetraethylenepentamine hydrochloride 28631-79-0, Aminoethylpiperazine 57578-49-1, Pentaethylenehexamine hydrochloride **62571-86-2**, Captopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transition metal chelators for inhibiting metal ion-dependent enzymes, and therapeutic use)

L67 ANSWER 10 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:681510 HCAPLUS
DOCUMENT NUMBER: 141:200192
TITLE: Methods and compositions using guanylate cyclase C receptor activators for the treatment of gastrointestinal disorders
INVENTOR(S): Currie, Mark G.; Mahajan-Miklos, Shalina
PATENT ASSIGNEE(S): Microbia, Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069165	A2	20040819	WO 2004-US2390	20040128 <--
WO 2004069165	A3	20050317		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2514507	AA	20040819	CA 2004-2514507		20040128 <--
EP 1594517	A2	20051116	EP 2004-706011		20040128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
PRIORITY APPLN. INFO.:			US 2003-443098P	P	20030128
			US 2003-471288P	P	20030515
			US 2003-519460P	P	20031112
			WO 2004-US2390	W	20040128

OTHER SOURCE(S): MARPAT 141:200192

AB The invention discloses compns. and related methods for treating irritable bowel syndrome (IBS) and other gastrointestinal disorders and conditions, e.g. gastrointestinal motility disorders, functional gastrointestinal disorders, gastroesophageal reflux disease (GERD), Crohn's disease, **ulcerative colitis**, **inflammatory bowel** disease, functional heartburn, dyspepsia (including functional dyspepsia or nonulcer dyspepsia), gastroparesis, chronic intestinal pseudo-obstruction (or colonic pseudo-obstruction), and disorders and conditions associated with constipation, e.g., constipation associated with use of opiate pain killers, post-surgical constipation, and constipation associated with neuropathic disorders as well as other conditions and disorders using peptides and other agents that activate the guanylate cyclase C (GC-C) receptor.

IC ICM A61K

CC 1-9 (Pharmacology)

IT **Intestine, disease**
(**inflammatory**; guanylate cyclase C receptor activators for treatment of gastrointestinal disorders)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; guanylate cyclase C receptor activators for treatment of gastrointestinal disorders)

IT 9015-82-1, **Angiotensin-converting** enzyme 9068-52-4, CGMP Phosphodiesterase 37255-34-8, 5α-Reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; guanylate cyclase C receptor activators for treatment of gastrointestinal disorders)

L67 ANSWER 11 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:589364 HCAPLUS
DOCUMENT NUMBER: 141:117196
TITLE: Nitrosated and nitrosylated rapamycin compounds, compositions and methods of use
INVENTOR(S): Garvey, David S.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060283	A2	20040722	WO 2003-US39562	20031215 <--

WO 2004060283 A3 20050324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2005209266 A1 20050922 US 2005-135308 20050524
PRIORITY APPLN. INFO.: US 2002-433595P P 20021216
US 2003-513215P P 20031023
WO 2003-US39562 A1 20031215

OTHER SOURCE(S): MARPAT 141:117196

AB The invention describes novel nitrosated and/or nitrosylated rapamycin compds., and novel compns. comprising at least one nitrosated and/or nitrosylated rapamycin compound, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The invention also provides novel compns. comprising at least one rapamycin compound and at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The compds. and compns. of the invention can also be bound to a matrix. The invention also provides methods for treating and/or preventing cardiovascular diseases, for the prevention of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating and/or preventing pathol. conditions resulting from abnormal cell proliferation; transplantation rejections; autoimmune, inflammatory, proliferative, hyperproliferative or vascular diseases; for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis by administering nitrosated and/or nitrosylated rapamycin compds. or rapamycin compds. in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions.

IC ICM A61K
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
IT **Intestine, disease**
(**inflammatory**; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)
IT 9015-82-1, **Angiotensin converting** enzyme 9015-94-5, Renin, biological studies 82707-54-8, Neutral endopeptidase 329900-75-6, Cyclooxygenase 2 433935-36-5, Polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

L67 ANSWER 12 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:392331 HCAPLUS
DOCUMENT NUMBER: 140:406798
TITLE: Preparation of benzoxepinopyridines as HMG-CoA

reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 875,155, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004092573	A1	20040513	US 2003-602752		20030624 <--
US 6812345	B2	20041102			
US 2002013334	A1	20020131	US 2001-875155		20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P	20000615
			US 2001-875155	B2	20010606

OTHER SOURCE(S): MARPAT 140:406798
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.
IC ICM A61K031-40
INCL 514423000
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT **Stomach, disease**
(**ulcer**, treatment; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide 58-32-2, Dipyridamole 58-93-5, Hydrochlorothiazide 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 564-25-0, Doxycycline 637-07-0, Clofibrate 657-24-9, Metformin 1684-40-8, Tacrine hydrochloride 3416-24-8, Glucosamine 4205-91-8, Clonidine hydrochloride 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin sulfate 10118-90-8, Minocycline 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 29094-61-9, Glipizide 29122-68-7, Atenolol 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose 56211-40-6, Torasemide **62571-86-2**, Captopril 68475-42-3, Anagrelide 72432-03-2,

Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 113665-84-2, Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 143653-53-6, Abciximab 144288-97-1, TS 962 144494-65-5, Tirofiban 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, 1750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Vioxx 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440 169590-42-5, Celebrex 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 188627-80-7, Eptifibatide 196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 246852-12-0, Amlodipine mesylate 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4, Rosuvastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 430433-43-5, CP644673 444069-80-1, Axokine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 13 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80450 HCAPLUS

DOCUMENT NUMBER: 140:145835

TITLE: Preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of the glucocorticoid receptor

INVENTOR(S): Vaccaro, Wayne; Yang, Bingwei Vera; Kim, Soong-hoon; Huynh, Tram; Tortolani, David R.; Leavitt, Kenneth J.; Li, Wenying; Doweyko, Arthur M.; Chen, Xiao-tao; Doweyko, Lidia

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.

SOURCE: PCT Int. Appl., 265 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

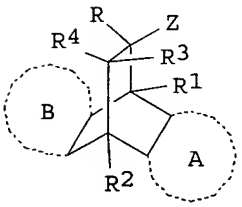
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009017	A2	20040129	WO 2003-US22300	20030717 <--
WO 2004009017	A3	20040708		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

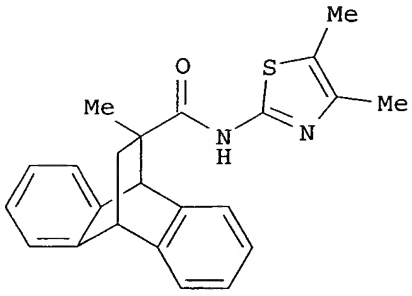
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004132758	A1	20040708	US 2003-621909		20030717 <--
EP 1534273	A2	20050601	EP 2003-765638		20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
NO 2005000074	A	20050309	NO 2005-74		20050106
US 2005171136	A1	20050804	US 2005-85347		20050321
PRIORITY APPLN. INFO.:			US 2002-396877P	P	20020718
			US 2003-621909	A1	20030717
			WO 2003-US22300	W	20030717

OTHER SOURCE(S): MARPAT 140:145835
GI



I



II

AB Title compds. I [R-R4 = H, alk(en/yn)yl, alkoxy, aryl, etc.; Z = carboxamido, alkylamino, etc.] are prepared For instance, 2-amino-4,5-dimethylthiazole is coupled to the acid derived from the cycloaddn. of methacrylic acid and anthracene (CH3CN, EDCI, Et3N, HOAt, 18 h) to give II. I are glucocorticoid receptor modulators which are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes, inflammatory and immune disorders.

IC ICM A61K

CC 24-7 (Alicyclic Compounds)
Section cross-reference(s): 1, 63

IT **Intestine, disease**
(**inflammatory**; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT Addison's disease
Adrenal gland, disease
Anemia (disease)
Antiarthritics
Antiasthmatics
Antirheumatic agents
Asthma
Atherosclerosis

Autoimmune disease
Behcet's syndrome
Blood, disease
Celiac disease
Connective tissue, disease
Dermatitis
Dermatomyositis
Diabetes insipidus
Diabetes mellitus
Digestive tract, disease
Eczema
Endocrine system, disease
Eye, disease
Gout
Graves' disease
Hay fever
Hepatitis
Human
Inflammation
Leukemia
Lymphoma
Multiple sclerosis
Myasthenia gravis
Neoplasm
Obesity
Osteoarthritis
Psoriasis
Respiratory system, disease
Rheumatic diseases
Rheumatoid arthritis
Seborrhea
Sepsis
Sjogren's syndrome
Skin, disease
Transplant rejection
(preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-78-2, Aspirin 51-21-8, 5-Fluorouracil 51-64-9, Dexamphetamine 52-24-4, Thiotepa 52-53-9, Verapamil 53-03-2, Prednisone 53-86-1, Indomethacin 58-32-2, Dipyridamole 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 67-78-7, Triamcinolone diacetate 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 5536-17-4, Vidarabine 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15687-27-1, Ibuprofen 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 36322-90-4, Piroxicam 41575-94-4, Carboplatin 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 59277-89-3, Aciclovir **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3,

Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 82410-32-0, Ganciclovir **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 104987-11-3, FK-506 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 136470-78-5, Abacavir 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Rofecoxib 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169590-42-5, Celecoxib 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4, GI 262570 199113-98-9, NN 2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT 9015-82-1, **Angiotensin-converting** enzyme

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitors**, combination pharmaceutical; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

L67 ANSWER 14 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 HCAPLUS
DOCUMENT NUMBER: 140:117406
TITLE: Liquid dosage compositions of stable nanoparticulate drugs
INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian
PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716 <--
WO 2004006959	C1	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2492488	AA	20040122	CA 2003-2492488		20030716 <--
EP 1551457	A1	20050713	EP 2003-764723		20030716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005536512	T2	20051202	JP 2004-521891		20030716
PRIORITY APPLN. INFO.:			US 2002-396530P	P	20020716
			WO 2003-US22187	W	20030716

AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

IC ICM A61K047-02
ICS A61K047-10; A61K047-26; A61K009-10; A61K009-14; A61K031-192; A61K031-58

CC 63-6 (Pharmaceuticals)

IT **Intestine, disease**
(**inflammatory**; liquid dosage compns. of stable nanoparticulate drugs)

IT 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-53-3, Chlorpromazine, biological studies 50-78-2, Acetylsalicylic acid 50-99-7, Glucose, biological studies 52-53-9, Verapamil 56-81-5, Glycerol, biological studies 56-85-9, Glutamine, biological studies 57-09-0, Hexadecyltrimethylammonium bromide 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 57-88-5, Cholesterol, biological studies 58-32-2, Dipyridamole 59-30-3, Folic acid, biological studies 62-49-7D, Choline, esters 63-42-3, Lactose 64-17-5, Ethanol, biological studies 67-45-8, Furazolidone 69-65-8, Mannitol 69-89-6D, Xanthine, derivs. 73-31-4, Melatonin 75-65-0, biological studies 80-74-0, Acetylsulfisoxazole 87-99-0, Xylitol 99-20-7, Trehalose 102-71-6, Triethanolamine, biological studies 110-86-1D, Pyridine, quaternized, salts 112-00-5, Lauryltrimethylammonium chloride 123-03-5, CPC 129-03-3, Cyproheptadine 132-17-2, Benztropine mesylate 134-32-7D, 1-Naphthylamine, alkyldimethylammonium salts 139-07-1, Lauryldimethylbenzylammonium chloride 140-72-7, Cetylpyridinium bromide 143-67-9, Vinblastine sulfate 148-79-8, Thiabendazole 151-21-3, SDS, biological studies 154-42-7, Thioguanine 288-32-4D, Imidazole, quaternized, salts 303-53-7, Cyclobenzaprine 396-01-0, Triamterene 500-92-5, Proguanil 502-65-8, Lycopene 645-05-6, Altretamine 846-50-4, Temazepam 1119-94-4, Dodecyltrimethylammonium bromide 1119-97-7, Tetradecyltrimethylammonium bromide 1200-22-2, Lipoic acid 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium Stearate 1643-19-2, Tetrabutylammonium bromide 1951-25-3, Amiodarone 1977-10-2, Loxapine 2062-78-4, Pimozide 2082-84-0, Decyltrimethylammonium bromide 2609-46-3, Amiloride 3416-24-8, Glucosamine 3458-28-4, Mannose

4205-90-7, Clonidine 4342-03-4, Dacarbazine 5137-55-3, Methyltrioctylammonium chloride 5350-41-4, Benzyltrimethylammonium bromide 7173-51-5, Dimethyldidecylammonium chloride 7281-04-1, Lauryldimethylbenzylammonium bromide 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride (MgCl2), biological studies 9000-01-5, Gum acacia 9000-30-0D, Guar gum, cationic derivs. 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Polyvinylpyrrolidone 9004-32-4 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hypromellose 9004-67-5, Methyl cellulose 9004-99-3, Polyethylene glycol stearate 9005-32-7, Alginic acid 9007-12-9, Calcitonin 9007-27-6, Chondroitin 9011-14-7, Poly(methyl methacrylate) 9011-14-7D, Poly(methyl methacrylate), hydrolyzed, trimethylammonium salts 9050-04-8, Cellulose, carboxymethyl ether, calcium salt 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10118-90-8, Minocycline 12441-09-7D, Sorbitan, esters 13292-46-1, Rifampin 16679-58-6, Desmopressin 18186-71-5, Dodecyltriethylammonium bromide 24280-93-1 25086-89-9, Vinyl acetate-1-vinyl-2-pyrrolidone copolymer 25301-02-4, Ethylene oxide-formaldehyde-4-(1,1,3,3-Tetramethylbutyl)phenol copolymer 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, phospholipid derivs. 26062-79-3, Poly(diallyldimethylammonium chloride) 27195-16-0, Sucrose distearate 27321-96-6, Polyethylene glycol cholesteryl ether 28228-56-0 28679-24-5, Dodecylbenzyltriethylammonium chloride 28981-97-7, Alprazolam 29094-61-9, Glipizide 29767-20-2, Teniposide 29836-26-8, n-Octyl-β-D-glucopyranoside 31431-39-7, Mebendazole 31566-31-1, Glyceryl monostearate 33419-42-0, Etoposide 34911-55-2, Bupropion 36735-22-5, Quazepam 37318-31-3, Sucrose stearate 38443-60-6, Decyltriethylammonium chloride 39809-25-1, Penciclovir 42399-41-7, Diltiazem 51264-14-3, Amsacrine 51569-39-2, Olin 10G 52128-35-5, Trimetrexate 52467-63-7, Tricetylmethylammonium chloride 55008-57-6 55268-75-2, Cefuroxime 55348-40-8, Triton X-200 58846-77-8, n-Decyl β-D-glucopyranoside 59080-45-4, n-Hexyl β-D-glucopyranoside 59122-55-3, n-DoDecyl β-D-glucopyranoside 59277-89-3, Acyclovir 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 69227-93-6, n-DoDecyl β-D-maltoside 69984-73-2, n-Nonyl β-D-glucopyranoside 70458-96-7, Norfloxacin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 73590-58-6, Omeprazole 76095-16-4, Enalapril maleate **76420-72-9**, Enalaprilat 76824-35-6, Famotidine 78617-12-6, n-Heptyl β-D-glucopyranoside 79617-96-2, Sertraline 79794-75-5, Loratadine 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81409-90-7, Cabergoline 81859-24-7, Polyquat 10 82494-09-5, n-Decyl β-D-maltoside 84449-90-1, Raloxifene 85261-19-4, Nonanoyl-N-methylglucamide 85261-20-7, Decanoyl-N-methylglucamide 85316-98-9 85618-20-8, n-Heptyl β-D-thioglucopyranoside 85618-21-9, n-Octyl-β-D-thioglucopyranoside 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole **87679-37-6**, Trandolapril 91161-71-6, Terbinafine 95233-18-4, Atovaquone 97322-87-7, Troglitazone 100286-97-3, Milrinone lactate 101397-87-9, D-Glucitol, 1-deoxy-1-[methyl(1-oxoheptyl)amino]- 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus 106266-06-2, Risperidone 106392-12-5, Pluronic 107397-59-1, Tetronic 150R8 110617-70-4, Poloxamine 113665-84-2, Clopidogrel 115956-12-2, Dolasetron 127666-00-6 127779-20-8, Saquinavir 132539-06-1, Olanzapine 136817-59-9, Delavirdine 138402-11-6, Irbesartan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 159989-65-8,

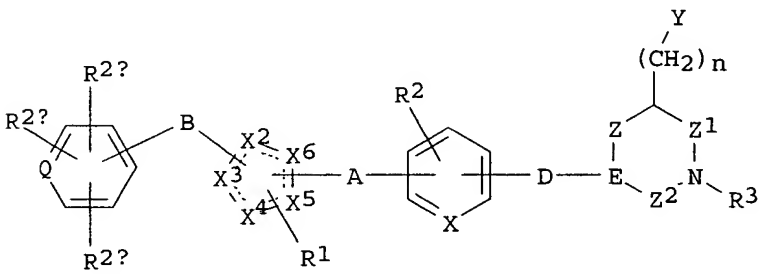
Nelfinavir mesylate 283158-20-3 329326-68-3, p-Isononylphenoxypolyglycidol 503178-50-5 608094-65-1, PEG-vitamin A 630400-66-7 630400-67-8 634601-99-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of stable nanoparticulate drugs)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 15 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41231 HCAPLUS
DOCUMENT NUMBER: 140:111429
TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik; Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung; Zhang, Hao; Wang, Wei; Ye, Xiang-Yang
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 543 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004665	A2	20040115	WO 2003-US22149	20030702 <--
WO 2004004665	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005536494	T2	20051202	JP 2004-520148	20030702
US 2004063700	A1	20040401	US 2003-616365	20030708 <--
NO 2005000077	A	20050203	NO 2005-77	20050106

PRIORITY APPLN. INFO.: US 2002-394508P P 20020709
WO 2003-US22149 W 20030702

OTHER SOURCE(S): MARPAT 140:111429
GI



I

AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3- (where X2, X3 = 0 to 5, provided that at least one of x2 and x3 is other than 0); B = a bond or (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6 = C, N, O, or S and at least one of X2-X6 is C; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halogen, (un)substituted amino; R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, etc.; E = CH, N; Z = (CH2)x5 (where x5 is 0, i.e. a single or a double bond, 1, 2), or Z is (CH2)x6 (where x6 = 2-5), where (CH2)x6 includes an alkenyl (C:C) bond embedded within the chain or Z = -(CH2)x7-O-(CH2)x8- (where x7, x8 = 0-4); (CH2)x to (CH2)x8, (CH2)m, (CH2)n, (CH2)p and (CH2)q may be optionally substituted; Y = CO2R4 (where R4 = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl or aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers, prodrug esters, and pharmaceutically acceptable salts thereof are prepared These compds., e.g. cis-1-ethoxycarbonyl-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidin-3-ylacetic acid and cis-1-(6-trifluoromethylpyrimidin-2-yl)-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidine-3-carboxylic acid, modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) levels, and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases employing such substituted acid derivs. alone or in combination with another antidiabetic agent and/or a hypolipidemic agent and/ or other therapeutic agents. Disclosed is a method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I. Also disclosed is a method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas and various other epithelial tumors (including breast, prostate, colon, ovarian, gastric and lung), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I.

IC ICM A61K

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **Stomach**, disease
(gastric **ulceritis**; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide

14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride
21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol
25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol
49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3,
Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril
72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin
75847-73-3, Enalapril **76547-98-3**, Lisinopril
79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin
85441-61-8, Quinapril **86541-75-5**, Benazepril
87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat
97240-79-4, Topiramate **98048-97-6**, Fosinopril
103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0,
Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate
113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4,
Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide
137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993
143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan
147511-69-1, Itavastatin 152755-31-2, LY295427 159183-92-3, L750355
160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1,
Ezetimibe 166518-60-1, Avasimibe 167305-00-2, Omapatrilat
168273-06-1, Rimonabant 169319-62-4, CGS 30440 170861-63-9, JTT-501
176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel
196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440
213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242
251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4, Visastatin
335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129
335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648
430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L67 ANSWER 16 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41224 HCAPLUS
DOCUMENT NUMBER: 140:111417
TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Ding, Charles Z.; Herpin, Timothy F.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004655	A2	20040115	WO 2003-US21331	20030708 <--
WO 2004004655	A3	20041014		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2490972	AA	20040115	CA 2003-2490972	20030708 <--
US 2004063762	A1	20040401	US 2003-616283	20030708 <--
US 6875782	B2	20050405		
EP 1531810	A2	20050525	EP 2003-763345	20030708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
NO 2004005529	A	20050203	NO 2004-5529	20041217
US 2005119312	A1	20050602	US 2004-16183	20041217

PRIORITY APPLN. INFO.:

US 2002-394553P	P	20020709
US 2003-616283	A3	20030708
WO 2003-US21331	W	20030708

OTHER SOURCE(S): MARPAT 140:111417

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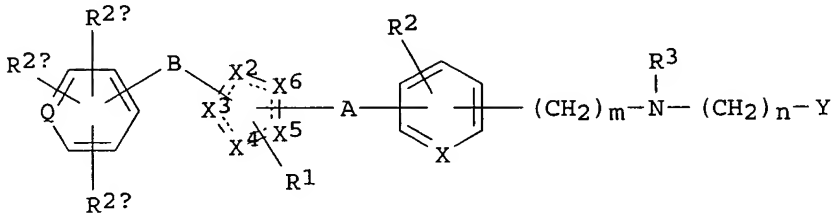


I

AB Compds. having general structure (I) [Q = C, N; A = (un)substituted (CH2)x (where x = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A = (un)substituted -(CH2)x2-O-(CH2)x3- (where x2, x3 = 0-5, provided that at least one of x2 and x3 is other than 0); B = a bond, (un)substituted (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6= C, N, O, or S, provided that at least one of X2-X6 is N; and at least one of X2, X3, X4, X5 and X6 is C; R1 = H, alkyl; R2, R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, etc.; Y = CO2R (where R = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl, aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof are prepared These compds. such as N-[[4-(1,2,3-triazol-4-ylmethoxy)benzyl](4-methoxypheoxycarbonyl)amino]acetic acid N-[[4-[2-(1,2,3-triazol-4-yl)ethoxy]benzyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(2- or 4-imidazolylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(1,2,4-oxadiazol-3-ylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[4-(1,2,4-oxadiazol-3-ylmethoxy)phenethyl](isobutoxycarbonyl)amino]acetic acid derivs. modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases.

IC ICM A61K
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT **Stomach**, disease
(gastric **ulceritis**; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe 166518-60-1, Avasimibe 168273-06-1, Rimonabant 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, ARHO 39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L67 ANSWER 17 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:950839 HCAPLUS
DOCUMENT NUMBER: 140:696
TITLE: Combination of a DPP IV inhibitor and a cardiovascular compound
INVENTOR(S): Holmes, David Grenville; Shetty, Suraj Shivappa; Hughes, Thomas Edward
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003099279	A1	20031204	WO 2003-EP5639	20030528 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2487167	AA	20031204	CA 2003-2487167	20030528 <--
EP 1511484	A1	20050309	EP 2003-755149	20030528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011397	A	20050315	BR 2003-11397	20030528
JP 2005532330	T2	20051027	JP 2004-506803	20030528
NO 2004005557	A	20050228	NO 2004-5557	20041220
PRIORITY APPLN. INFO.:			GB 2002-12412 A	20020529
			WO 2003-EP5639 W	20030528

AB The invention relates to a combination therapy, such as a combined preparation or pharmaceutical composition, resp., comprising of a DPP IV inhibitor or a pharmaceutically acceptable salt thereof and a cardiovascular compound (being different from a statin) or a pharmaceutically acceptable salt thereof. The invention furthermore relates to the use of such a combination for the prevention, delay of progression or treatment of diseases and disorders selected from the group consisting of hypertension, congestive heart failure, left ventricular hypertrophy, peripheral arterial disease, diabetes, especially type 2 diabetes mellitus, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulosclerosis, chronic renal failure, diabetic neuropathy, syndrome X, premenstrual syndrome, coronary heart disease, angina pectoris, thrombosis, atherosclerosis, myocardial infarction, transient ischemic attacks, stroke, vascular restenosis, hyperglycemia, hyperinsulinemia, hyperlipidemia, hypertrygliceridemia, insulin resistance, impaired glucose metabolism, conditions of impaired glucose tolerance, conditions of impaired fasting plasma glucose, obesity, erectile dysfunction, skin and connective tissue disorders, foot **ulcerations** and **ulcerative colitis**, endothelial dysfunction and impaired vascular compliance.

IC ICM A61K031-454
ICS A61K031-40; A61K031-16; A61P003-10; A61K031-41

CC 1-4 (Pharmacology)
Section cross-reference(s): 63

IT 9015-82-1, **Angiotensin converting** enzyme 9015-94-5, Renin, biological studies 54249-88-6, DPP IV 82707-54-8, Neutral endopeptidase 122933-89-5, Aldosterone synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combination of DPP IV **inhibitor** and cardiovascular compound)

IT 58-93-5, Hydrochlorothiazide 51384-51-1, Metoprolol 74191-85-8, Doxazosin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 88150-42-9, Amlodipine 102676-47-1, Fadrozole 102676-87-9, (+)-Fadrozole 107724-20-9, Eplerenone 112573-73-6, Sinorphan 114798-26-4, Losartan 123122-55-4, Candoxatril 137862-53-4, Valsartan 144689-24-7, Olmesartan 147536-97-8, Bosentan 167305-00-2, Omapatrilat 173334-57-1, Aliskiren 247016-69-9 274901-16-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of DPP IV inhibitor and cardiovascular compound)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L67 ANSWER 18 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:845158 HCAPLUS
DOCUMENT NUMBER: 140:314987
TITLE: Pro-inflammatory Effect of Quercetin by Dual **Blockade** of **Angiotensin Converting**-enzyme and Neutral Endopeptidase In Vivo
AUTHOR(S): Nicolau, M.; Dovichi, S. s.; Cuttle, G.
CORPORATE SOURCE: Dept. de Ciencias Fisiologicas, Centro di Ciencias Biologicas, Univ. Federal de Santa Catarina, Florianopolis, 88040-900, Brazil
SOURCE: Nutritional Neuroscience (**2003**), 6(5), 309-316
CODEN: NNINFE; ISSN: 1028-415X
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of the flavonoid quercetin on substance P- and bradykinin-induced plasma extravasation in rat tissues (duodenum, heart, pancreas, trachea and urinary bladder) was studied, and its modulation by endogenous peptidases. Plasma protein extravasation was assayed by extravasated Evans blue dye. I.v. injection of substance P (1, 3 and 10 nmol/kg) increased the plasma extravasation in a dose-dependent manner in heart, pancreas, trachea and urinary bladder. Bradykinin (3 and 10 nmol/kg, i.v.) increased plasma extravasation in a dose-dependent manner in duodenum, pancreas, trachea and urinary bladder. Pre-treatment with a selected dose of quercetin potentiated the substance P-induced plasma extravasation in heart, pancreas and urinary bladder, and also the bradykinin-induced plasma extravasation in duodenum, heart, trachea and urinary bladder. The selective pharmacol. **inhibition** of neutral endopeptidase and **angiotensin-converting** enzyme potentiated the substance P- and bradykinin-induced plasma extravasation, resp.; furthermore, treatment with receptor **antagonists** showed that the mediators involved in the potentiation of plasma extravasation by quercetin are substance P and bradykinin. Anal. of plasma **angiotensin-converting** enzyme activity demonstrated that quercetin **inhibited** this enzyme. These results suggest that quercetin potentiates plasma extravasation induced by substance P and bradykinin, and that this may result from inhibition of the degradative enzymes of these peptides.

CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 18

IT **Intestine**
(duodenum; pro-**inflammatory** effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

IT Blood vessel
(permeability; pro-inflammatory effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

IT Biological transport
(permeation, vascular; pro-inflammatory effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

IT Bladder
Heart
Inflammation

Pancreas
Trachea (anatomical)
(pro-inflammatory effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

IT 117-39-5, Quercetin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pro-inflammatory effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

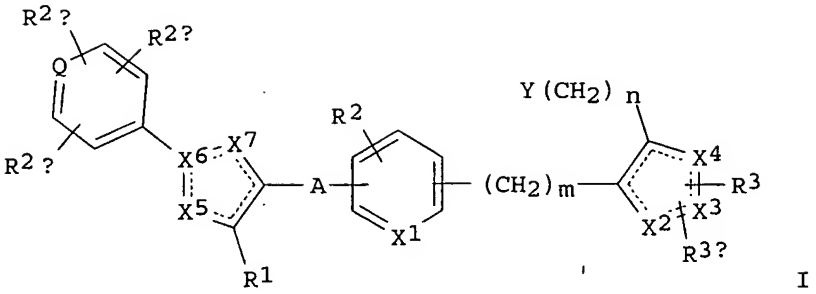
IT 58-82-2, Bradykinin 9015-82-1, **Angiotensin-converting** enzyme 33507-63-0, Substance P peptide 82707-54-8, Neutral endopeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pro-inflammatory effect of quercetin by dual **blockade** of **angiotensin converting**-enzyme and neutral endopeptidase in rat tissue)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 19 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:656421 HCAPLUS
DOCUMENT NUMBER: 139:197489
TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 153,454.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 2003158232	A1	20030821	US 2002-294525		20021114	<--
US 6967212	B2	20051122				
US 2003092736	A1	20030515	US 2002-153454		20020522	<--
US 2005124661	A1	20050609	US 2004-12810		20041215	
PRIORITY APPLN. INFO.:			US 2001-294380P	P	20010530	
			US 2002-153454	A2	20020522	
			US 2002-294525	A3	20021114	

OTHER SOURCE(S): MARPAT 139:197489
GI



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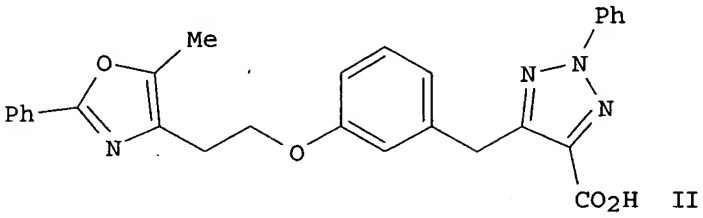


II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; ≥1 of x2, x3 ≠ 0; X1 = CH, N; X2, X3, X4, X5, X7 = C, N, O, S; in each of X1-X7, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b and R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3, R3a = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPARγ) and stimulators of peroxisome proliferator activated receptor-α (PPARα). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPARα and to PPARγ ligand binding domains with IC50 = 69 nM.

IC ICM A61K031-444
ICS A61K031-4439; A61K031-427; A61K031-422; C07D417-02; C07D417-14; C07D413-14; C07D413-02

INCL 514333000; 514340000; 514341000; 514342000; 514367000; 514375000; 514397000; 546256000; 546269700; 546271400

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Stomach, disease**
(**ulcer**, treatment; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

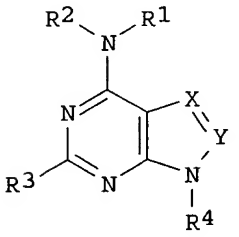
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril

76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 143443-90-7, Ifetroban 144288-97-1, Ts-962 145599-86-6, Cerivastatin 152755-31-2, Ly295427 159183-92-3, 1750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, Cgs 30440 170861-63-9, Jtt-501 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9 199914-96-0, Ym-440 213252-19-8, Krp297 244081-42-3, Aj9677 251572-86-8, p32/98 282526-98-1, Atl-962 287714-41-4, Visastatin 335149-08-1, 1895645 335149-14-9, r-119702 335149-15-0, Kad1129 335149-17-2, Arho39242 335149-19-4, Gw-409544 335149-23-0, Nvp-dpp-728a 335149-25-2, Cp331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

L67 ANSWER 20 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:570644 HCAPLUS
DOCUMENT NUMBER: 139:133575
TITLE: Preparation of bicyclic pyrimidinyl derivatives as adenosine receptor ligands
INVENTOR(S): Castelhano, Arlindo L.; McKibben, Bryan
PATENT ASSIGNEE(S): OSI Pharmaceuticals Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 105 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003139427	A1	20030724	US 2002-227378	20020823 <--
PRIORITY APPLN. INFO.:			US 2002-227378	20020823

OTHER SOURCE(S): MARPAT 139:133575
GI



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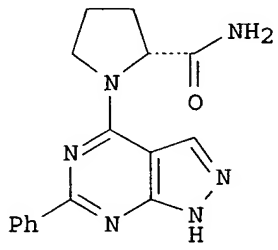


II

AB Title compds. I [Y = N, CR5 and X = N, CR6 wherein X, Y are both N or when Y = CR5, X = N or when X = CR6, Y = N; R1-2 = H, alkoxy, aminoalkyl, etc; R3-4 = H, alkyl, aryl, alkylaryl] are prepared For instance, 3-amino-4-carbamoylpyrazole is acylated with benzoyl chloride (Pyridine, 50°, 5-6 h), cyclized to the corresponding pyrazolopyrimidine (water, K2CO3, 100°, 16 h), converted to the chloride (POCl3, 106°, 2 h) and used for reactions with various amines to give the example compds., e.g., II. II has Ki = 76.7 nM for the adenosine A1 receptor, Ki = 242.7 nM for A2a and Ki = 1480.5 nM for A2b. I are useful for the treatment of.

IC ICM C07D487-02
ICS A61K031-52; A61K031-519

INCL 514261100; 514262100; 514263200; 514263400; 544277000; 544262000; 544254000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **Intestine, disease**
(**inflammatory**; preparation of bicyclic pyrazolo- imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; preparation of bicyclic pyrazolo-imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

IT 9015-82-1, **Angiotensin-converting** enzyme
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitors**, combination pharmaceutical; preparation of bicyclic pyrazolo- imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

L67 ANSWER 21 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:132967 HCAPLUS
DOCUMENT NUMBER: 138:163546
TITLE: Methods and compositions for treating diseases associated with excesses in ACE
INVENTOR(S): Moskowitz, David W.
PATENT ASSIGNEE(S): Genomed, LLC, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013434	A2	20030220	WO 2002-US25001	20020806 <--
WO 2003013434	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2005503378	T2	20050203	JP 2003-518448		20020806
PRIORITY APPLN. INFO.:			US 2001-310064P	P	20010806
			US 2002-347013P	P	20020111
			US 2002-347905P	P	20020115
			US 2002-350563P	P	20020124
			US 2002-352072P	P	20020128
			US 2002-352074P	P	20020128
			US 2002-352484P	P	20020130
			US 2002-378467P	P	20020508
			US 2002-379796P	P	20020513
			US 2002-380741P	P	20020516
			WO 2002-US25001	W	20020806

AB Over 40 common diseases, in addition to congestive heart failure (CHF) due to hypertension (HTN) or non-insulin dependent diabetes mellitus (type II diabetes mellitus) (NIDDM), atherosclerotic peripheral vascular disease (ASPVD) due to HTN or NIDDM, and chronic obstructive pulmonary disease; emphysema (COPD), are associated with the ACE D/D genotype and should also respond to an adequate tissue-ID of **ACE inhibitors** such as quinapril. Several of these diseases have now been successfully treated using higher than normal dosages of **ACE inhibitors**, especially hydrophobic **ACE inhibitors**, with good outcomes. **ACE inhibitors** have also been found to be useful in inhibiting apoptosis and aging in general. Dosages that have been utilized are typically greater than quinapril at a dose of 40 to 80 mg/day, i.e. up to 1 mg/kg per day for a "typical" 80 kg patient. New formulations of **ACE inhibitors** have been developed for these higher dosages, including 80 mg tablets, controlled and/or sustained release formulations, and formulations containing a second active agent such as a diuretic, or a compound such as furosemide 20 mg/day (for creatinine <2.5 mg/dL) or furosemide 40 mg/day (for creatinine >2.5 mg/dL), to prevent fluid retention and congestive heart failure in patients with renal failure. The **ACE inhibitors** can also be combined with an angiotensin receptor blocker.

IC ICM A61K

CC 1-8 (Pharmacology)
Section cross-reference(s): 7, 63

ST disease assocd excess angiotensin converting enzyme treatment; **ACE inhibitor** dosage disease treatment; formulation **ACE inhibitor**

IT Hepatitis
(A, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Feed
(**ACE inhibitor** administration in; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Allergy inhibitors
Anti-AIDS agents
Anti-Alzheimer's agents
Antiasthmatics
Antidepressants
Antiglaucoma agents
Antihypertensives
Antiobesity agents
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
Antiulcer agents
Anxiolytics

Drug delivery systems
Human
Human groups
Tuberculostatics
(**ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Blood serum
(**ACE inhibitor** in combination with fludrocortisone acetate in relation to potassium ion concentration in; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Angiotensin receptor antagonists
Diuretics
(**ACE inhibitor** in combination with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Hepatitis
(B, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Genotypes
(D/D of ACE DCP1 gene, diseases in relation to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DCP1, for ACE, D/D genotype, diseases in relation to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Kidney, disease
(HIV-associated, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Kidney, disease
(IgA nephropathy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Bone, disease
(Paget's, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Drugs of abuse
(abuse of, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Tobacco smoke
(abuse, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Blood vessel
(access in end-stage renal disease; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Inflammation
Reproductive system, disease
(adnexitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Hepatitis
(alc., treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Allergy
Inflammation
Nose, disease
(allergic rhinitis, treatment of; **ACE inhibitor**

dosages and formulations for treating diseases associated with excesses in ACE)
IT Angiotensin receptor antagonists
(angiotensin II, **ACE inhibitor** in combination with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Antiarteriosclerotics
(antiatherosclerotics; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Disease, animal
(associated with excess ACE, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Skin, neoplasm
(basal cell carcinoma, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Carcinoma
(basal cell, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Mental and behavioral disorders
(bipolar disorder; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Gallbladder, disease
Inflammation
(cholecystitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Lung, disease
(chronic obstructive, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Drug delivery systems
(controlled-release; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Kidney, disease
(cyst, acquired renal cystic disease of end-stage renal disease, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Mental and behavioral disorders
(dementia, multi-infarct, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Mental and behavioral disorders
(dementia, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Mental and behavioral disorders
(depression, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Nerve, disease
(diabetic neuropathy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Eye, disease
(diabetic retinopathy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Joint, anatomical
(disease, degeneration, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in

ACE)
IT **Inflammation**
Intestine, disease
(**diverticulitis**, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Intestine, disease
(diverticulosis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Lung, disease
(embolism, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hypertension
(end-stage renal disease with, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Kidney, disease
(failure, chronic, irreversible, with hypertension or type II diabetes, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Kidney, disease
(failure, due to hypertension or type II diabetes, delay progression of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Kidney, disease
(focal segmental glomerulonephritis, end-stage renal disease due to, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hip
(fractures, prevention of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Stomach, disease
(gastritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Digestive tract, disease
(gastroesophageal reflux, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Infection
(hepatitis A, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Infection
(hepatitis B, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Musculoskeletal diseases
(hernia, hiatal or inguinal hernia, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Lipids, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT **Intestine, disease**
(**inflammatory**, treatment of; **ACE inhibitor**

dosages and formulations for treating diseases associated with excesses in ACE)
IT Animal tissue
(inhibition of ACE of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Apoptosis
(inhibition of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Intestine, disease
(irritable bowel syndrome, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Brain, disease
(ischemia, transient, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Disease, animal
(joint degeneration, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Heart, disease
(left ventricle, hypertrophy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hypertrophy
(left ventricular, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Kidney, disease
(membranous glomerulonephritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Kidney, disease
(mesangial proliferative glomerulonephritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Headache
(migraine, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Diabetes mellitus
(non-insulin-dependent, end-stage renal disease with, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Kidney, disease
(obstructive uropathy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hydrophobicity
(of **ACE inhibitor**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Pancreas, disease
(pancreatitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Ulcer
(peptic, treatment of; **ACE inhibitor** dosages and

formulations for treating diseases associated with excesses in ACE)
IT Blood vessel, disease
(peripheral, atherosclerotic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hearing loss
(presbycusis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Aging, animal
(progressive loss of hearing in, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Embolism
Hypertension
(pulmonary, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Cyst, pathological
(renal, acquired renal cystic disease of end-stage renal disease, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Nose, disease
(rhinitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Connective tissue, disease
(scleroderma, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Inflammation
Respiratory system, disease
(sinusitis, allergic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Neoplasm
(solid, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Brain, disease
(stroke, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Drug delivery systems
(sustained-release; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Lupus erythematosus
(systemic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Drug delivery systems
(tablets, chewable; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Drug delivery systems
(tablets; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Hyperparathyroidism
(tertiary, in end-stage renal disease, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Drug allergy
(to penicillin or sulfa, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
IT Ischemia

(transient cerebral, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Human immunodeficiency virus
(treatment of infection with or complications of infection with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Animal
(treatment of non-human; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT AIDS (disease)
Allergy
Alzheimer's disease
Anxiety
Ascites
Asthma
Atherosclerosis
Calculi, biliary
Calculi, renal
Cataract
Cirrhosis
Eczema
Emphysema
Glaucoma (disease)
Gout
Headache
Hypercholesterolemia
Hypertriglyceridemia
Hypothyroidism
Leukemia
Lymphoma
Obesity
Osteoarthritis
Osteoporosis
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Schizophrenia
Seizures
Tuberculosis
(treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Digestive tract, disease
(ulcer, peptic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT Thrombosis
(venous, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 514-36-3, Fludrocortisone acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ACE inhibitor** administration in combination with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT **62571-86-2**, Captopril **75847-73-3**, Enalapril **76547-98-3**, Lisinopril **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 52-39-1, Aldosterone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration with **ACE inhibitor**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 9015-82-1, **Angiotensin-converting** enzyme
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 24203-36-9, Potassium ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of serum, **ACE inhibitor** in combination with fludrocortisone acetate in relation to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 127-31-1, Florinef
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinapril with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 1406-05-9, Penicillin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(treatment of allergy to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

IT 57-88-5, Cholesterol, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of high levels of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

L67 ANSWER 22 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:80434 HCAPLUS
DOCUMENT NUMBER: 138:180722
TITLE: Method for the treatment of gastric ulcer disease in patients with decreased gastric secretion
INVENTOR(S): Medvedev, V. N.; Ivkova, I. A.
PATENT ASSIGNEE(S): Ivanovskaya Gosudarstvennaya Meditsinskaya Akademiya, Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2188010	C2	20020827	RU 2000-110867	20000427 <--
PRIORITY APPLN. INFO.:			RU 2000-110867	20000427

AB Method is disclosed for the treatment of gastric ulcer disease in patients with decreased gastric acid secretion. Method involves treatment with ranitidine at half of a dose of 75 mg/d together with captopril (**capoten**) at the dose of 12.5 mg twice daily for a month. Method provides a purposeful action upon the processes of ulcer reparation. Method ensures higher efficiency of treatment.

IC ICM A61K031-341
ICS A61K031-401; A61P001-04
CC 1-9 (Pharmacology)
ST ranitidine captopril antiulcer human gastric ulcer disease; **capoten** ranitidine gastric acid hyposecretion **stomach** **ulcer** disease human
IT **Stomach**
(antrum, gastric **ulcer** localized in; method for treatment of gastric ulcer disease in patients with decreased gastric secretion)
IT Inflammation
Stomach, disease
(atrophic gastritis; method for treatment of gastric **ulcer** disease in patients with decreased gastric secretion)
IT **Stomach**
(fundus, gastric **ulcer** localized in; method for treatment of gastric ulcer disease in patients with decreased gastric secretion)
IT **Stomach**
(pylorus, gastric **ulcer** localized in; method for treatment of gastric ulcer disease in patients with decreased gastric secretion)
IT **Stomach, disease**
(**ulcer**; method for treatment of gastric **ulcer** disease in patients with decreased gastric secretion)
IT **62571-86-2**, Captopril 66357-35-5, Ranitidine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of gastric ulcer disease in patients with decreased gastric secretion)

L67 ANSWER 23 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:978628 HCAPLUS
DOCUMENT NUMBER: 138:49938
TITLE: Nucleic acids for the prevention and treatment of gastric ulcers
INVENTOR(S): Bratzler, Robert L.; Petersen, Deanna M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002198165	A1	20021226	US 2001-920313		20010801 <--
PRIORITY APPLN. INFO.:			US 2000-222248P	P	20000801

OTHER SOURCE(S): MARPAT 138:49938
AB The invention relates to methods and products for treating gastric ulcers. A nucleic acid and optionally an anti-ulcer agent are administered to a subject to prevent or treat gastric ulcer.
IC ICM A61K048-00
INCL 514044000
CC 1-9 (Pharmacology)
IT **Stomach, disease**
(**ulcer**; nucleic acids for prevention and treatment of gastric ulcers in relation to immunostimulation and combination with other agents)
IT 35115-60-7, Teprotide **62571-86-2**, Captopril 63250-36-2, Epicaptopril **74258-86-9**, Alacepril 75107-57-2 75176-37-3,

Zofenoprilat 75479-46-8 **75847-73-3**, Enalapril 76095-16-4, Enapril **76420-72-9**, Enalaprilat **76547-98-3**, Lisinopril 78636-30-3 80828-34-8, Indolaprilat 80876-01-3, Indolapril 80943-05-1, Converstatin 81045-50-3, Pivalopril 81872-10-8, Zofenopril 82586-55-8, Quinapril hydrochloride **82768-85-2**, Quinaprilat **82834-16-0**, Perindopril 82924-03-6, Pentopril 83059-56-7, Zabicipril 83398-08-7 **83435-66-9**, Delapril 83602-05-5, Spiraprilat **83647-97-6**, Spirapril **85441-61-8**, Quinapril 85856-54-8, Moveltipril 85921-53-5, Altiopril calcium **86541-74-4**, Benazepril hydrochloride **86541-75-5**, Benazepril 86541-78-8, Benazeprilat 87269-97-4, Ramiprilat **87333-19-5**, Ramipril **87679-37-6**, Trandolapril 87679-71-8, Trandolaprilat 88201-41-6, Ancovenin **88768-40-5**, Cilazapril 88889-14-9 **89371-37-9**, Imidapril 90103-92-7, Zabiciprilat 90139-06-3, Cilazaprilat 90965-60-9, Muracein A 90965-61-0, Muracein B 91105-26-9, Muracein C 94841-17-5, Spirapril hydrochloride **95153-31-4**, Perindoprilat **95399-71-6**, Fosfenopril **98048-97-6**, Fosenopril 100157-28-6, Foroxymithine **103775-10-6**, Moexipril 103775-14-0, Moexiprilat 103930-64-9, Hemorphin-4 109214-55-3, Libenzapril 109683-61-6, Utibapril 110221-44-8, Temocapril hydrochloride **111223-26-8**, Ceranapril **111902-57-9**, Temocapril 113082-98-7, Enalkiren 125708-06-7, Lyciumin A 125756-66-3, Lyciumin B **127420-24-0**, Idrapril 135038-56-1, Glycopril 135038-57-2, Alatriopril 156039-69-9, Mixanpril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ACE inhibitor**; nucleic acids for prevention and treatment of gastric ulcers in relation to immunostimulation and combination with other agents)

IT 9015-82-1, **Angiotensin-converting** enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; nucleic acids for prevention and treatment of gastric ulcers in relation to immunostimulation and combination with other agents)

L67 ANSWER 24 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927185 HCAPLUS
DOCUMENT NUMBER: 138:24716
TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096358	A2	20021205	WO 2002-US16633	20020523 <--
WO 2002096358	A3	20030327		

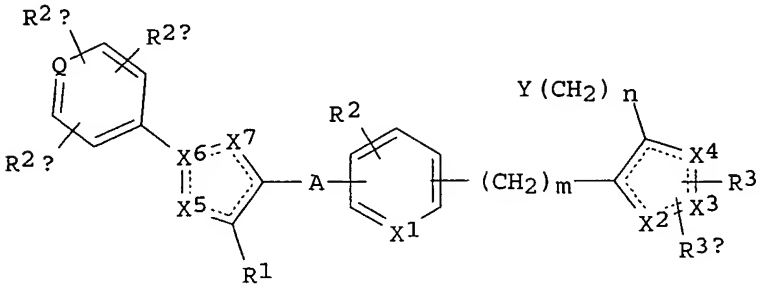
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449160	AA	20021205	CA 2002-2449160		20020523 <--
EP 1390363	A2	20040225	EP 2002-729306		20020523 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
TR 200400650	T3	20040621	TR 2004-200400650		20020523 <--
JP 2004536070	T2	20041202	JP 2002-592871		20020523 <--
PRIORITY APPLN. INFO.:			US 2001-294380P	P	20010530
			WO 2002-US16633	W	20020523

OTHER SOURCE(S): MARPAT 138:24716

GI



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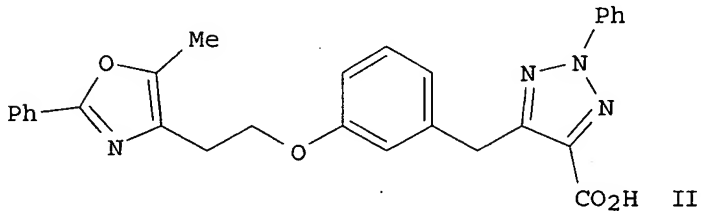


II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; ≥1 of x2, x3 ≠ 0; X1 = CH, N; X2, X3, X4, X5, X7 = C, N, O, S; in each of X1-X7, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b and R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3, R3a = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, alkyl(halo)aryloxycarbonyl, alkoxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aryloxyarylalkyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylsulfinylarylcarbonyl, etc.; Y = CO2R4,

1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPARγ) and stimulators of peroxisome proliferator activated receptor-α (PPARα). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPARα and to PPARγ ligand binding domains with IC50 = 69 nM.

IC ICM A61K

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **Stomach, disease**
(**ulcer**, treatment; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 143443-90-7, Ifetroban 144288-97-1, Ts-962 145599-86-6, Cerivastatin 152755-31-2, Ly295427 159183-92-3, l750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, Cgs 30440 170861-63-9, Jtt-501 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Nn-2344 199914-96-0, Ym-440 213252-19-8, Krp297 244081-42-3, Aj9677 251572-86-8, p32/98 282526-98-1, Atl-962 287714-41-4 335149-08-1, l895645 335149-14-9, r-119702 335149-15-0, Kad1129 335149-17-2, Arho39242 335149-19-4, Gw-409544 335149-23-0, Nvp-dpp-728a 335149-25-2, Cp331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

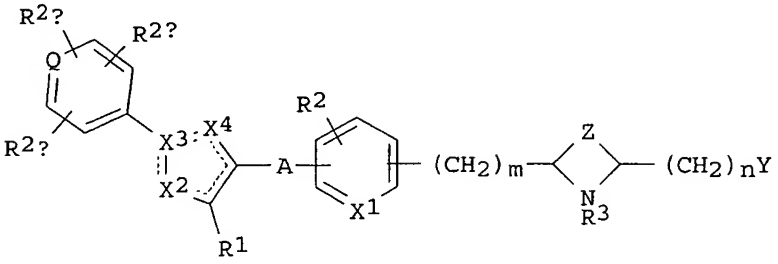
L67 ANSWER 25 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927184 HCAPLUS
DOCUMENT NUMBER: 138:14048
TITLE: Preparation of oxazolylethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.
INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523 <--
WO 2002096357	A3	20030925		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003092697	A1	20030515	US 2002-153342	20020522 <--
CA 2449006	AA	20021205	CA 2002-2449006	20020523 <--
EP 1401433	A2	20040331	EP 2002-737192	20020523 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005506954	T2	20050310	JP 2002-592870	20020523

PRIORITY APPLN. INFO.:
US 2001-294505P P 20010530
WO 2002-US16628 W 20020523

OTHER SOURCE(S): MARPAT 138:14048
GI



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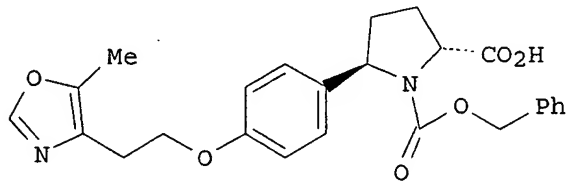


II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, with an alkenyl or alkynyl bond in the chain, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; provided that ≥1 of x2 and x3 ≠ 0; X1 = CH, N; X2 = C, N, O, S; X3 = C, N; X4 = C, N, O, S provided that ≥1 of X2, X3, X4 = N; in each of X1-X4, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl,

alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylaminoarylalkyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; Z = (CH2)x4, (CH2)x5, (CH2)x6O(CH2)x7; x4 = 1-5; x5 = 2-5; x6, x7 = 0-4], were prepared as antidiabetic and antiobesity agents (no data). Thus, title compound (II) was prepared in 6 steps.

IC ICM A61K

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34

IT **Stomach, disease**
(**ulcer**, treatment; preparation of oxazolylethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin **85441-61-8**, Quinapril **86541-75-5**, Benazepril **87333-19-5**, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**, Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4, GI 262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of oxazolylethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

L67 ANSWER 26 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:540258 HCAPLUS
DOCUMENT NUMBER: 137:109267
TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002094977	A1	20020718	US 2001-7407		20011204 <--
US 6627636	B2	20030930			
US 2002013334	A1	20020131	US 2001-875155		20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P	20000615
			US 2001-875155	A2	20010606

OTHER SOURCE(S): MARPAT 137:109267
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDl cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

IC ICM C07D498-02
ICS A61K031-55; A61K031-4745
INCL 514215000
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT **Stomach, disease**
(**ulcer**, treatment; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide 58-32-2, Dipyridamole 58-93-5, Hydrochlorothiazide 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 564-25-0, Doxycycline 637-07-0, Clofibrate 657-24-9, Metformin 1684-40-8, Tacrine hydrochloride 3416-24-8, Glucosamine 4205-91-8, Clonidine hydrochloride 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin sulfate 10118-90-8, Minocycline 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 29094-61-9, Glipizide 29122-68-7, Atenolol 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose 56211-40-6, Torasemide **62571-86-2**, Captopril 68475-42-3, Anagrelide 72432-03-2,

Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin
75847-73-3, Enalapril **76547-98-3**, Lisinopril
79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin
85441-61-8, Quinapril **86541-75-5**, Benazepril
87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat
97240-79-4, Topiramate 97322-87-7, Troglitazone **98048-97-6**,
Fosinopril **103775-10-6**, Moexipril 105816-04-4, Nateglinide
106650-56-0, Sibutramine 111025-46-8, Pioglitazone 113665-84-2,
Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil
122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1,
Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan
141758-74-9, AC2993 143443-90-7, Ifetroban 143653-53-6, Abciximab
144288-97-1, TS 962 144494-65-5, Tirofiban 145599-86-6, Cerivastatin
147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, l750355
160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Vioxx
166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440
169590-42-5, Celebrex 170861-63-9, JTT-501 176435-10-2, LY315902
178759-95-0, MD 700 182815-44-7, Cholestagel 188627-80-7, Eptifibatide
196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440
213252-19-8, KRP297 244081-42-3, AJ9677 246852-12-0, Amlodipine
mesylate 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4,
Rosuvastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0,
KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0,
NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride
430433-43-5, CP644673 444069-80-1, Axokine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

L67 ANSWER 27 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:157564 HCAPLUS
DOCUMENT NUMBER: 136:205424
TITLE: Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors
INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015892	A2	20020228	WO 2001-EP9586	20010820 <--
WO 2002015892	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002014952	A5	20020304	AU 2002-14952		20010820 <--
EP 1359907	A2	20031112	EP 2001-983442		20010820 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004519424	T2	20040702	JP 2002-520813		20010820 <--
US 2004087630	A1	20040506	US 2003-362341		20030618 <--
PRIORITY APPLN. INFO.:			US 2000-643642	A	20000822
			WO 2001-EP9586	W	20010820

AB The present invention relates to a combination, especially a pharmaceutical composition, comprising (a) an insulin secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) **ACE inhibitors** or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical composition, a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets containing nateglinide.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

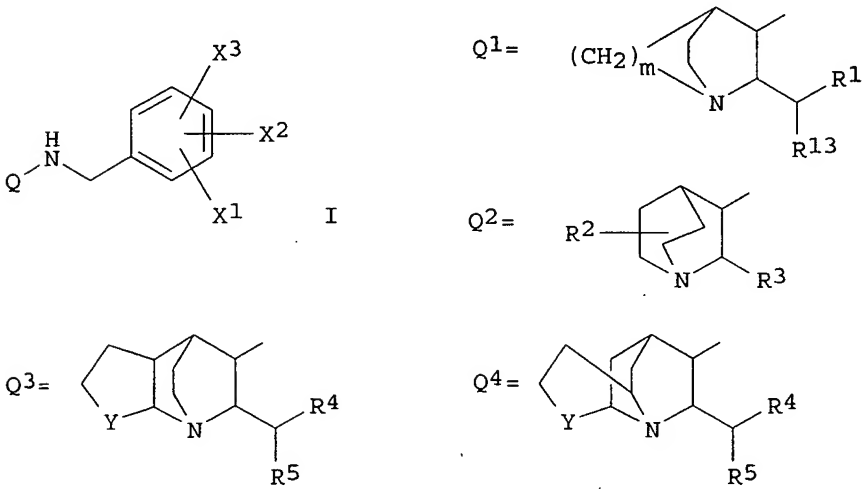
IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopyramide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone **62571-86-2**, Captopril **74258-86-9**, Alacepril 75330-75-5, Lovastatin **75847-73-3**, Enalapril **76420-72-9**, Enalaprilat **76547-98-3**, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin **82834-16-0**, Perindopril **83435-66-9**, Delapril **83647-97-6**, Spirapril **85441-61-8**, Quinapril 85856-54-8, Moveltipril **86541-75-5**, Benazepril 86541-78-8, Benazeprilat **87333-19-5**, Ramipril **87679-37-6**, Trandolapril **88768-40-5**, Cilazapril **89371-37-9**, Imidapril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin **98048-97-6**, Fosinopril 105816-04-4, Nateglinide **111223-26-8**, Ceronapril **111902-57-9**, Temocapril 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

L67 ANSWER 28 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:47520 HCAPLUS
DOCUMENT NUMBER: 136:102294
TITLE: Preparation of fluoroalkoxybenzylamino derivatives of nitrogen containing heterocycles as substance P

receptor antagonists
INVENTOR(S): Chappel, Phillip Branch; O'neill, Brian Thomas; Saltarelli, Mario David
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 1172106	A2	20020116	EP 2001-303983		20010501	<--
EP 1172106	A3	20020515				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
ZA 2001003484	A	20021202	ZA 2001-3484		20010430	<--
CA 2345760	AA	20011103	CA 2001-2345760		20010501	<--
JP 2002020287	A2	20020123	JP 2001-134144		20010501	<--
NZ 522391	A	20040827	NZ 2001-522391		20010502	<--
US 2002035147	A1	20020321	US 2001-848069		20010503	<--
US 2003114439	A1	20030619	US 2002-208274		20020729	<--
PRIORITY APPLN. INFO.:			US 2000-201591P	P	20000503	
			US 2000-237780P	P	20001004	
			NZ 2001-511453	A1	20010502	
			US 2001-848069	B1	20010503	

OTHER SOURCE(S): MARPAT 136:102294
GI



AB The present invention relates to methods of treating various central nervous system (CNS) and other disorders or conditions by administering fluoroalkoxybenzylamino derivs. of nitrogen containing heterocyclic compds., and specifically, by administering compds. of the formula [I; X1 = H, C1-10 alkoxy or alkyl optionally substituted with from one to three fluorine atoms; X2, X3 = halo, H, NO2, C1-10 alkyl or alkoxy optionally substituted with from one to three fluorine atoms, CF3, hydroxy, Ph,

cyano, amino, C1-6 alkylamino, di(C1-6 alkyl)amino, -CONH-C1-6alkyl, C1-6 alkyl-CONH-C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, NHCHO, NHCO-C1-C6 alkyl; Q = N-containing heterocyclyl, e.g. Q1, Q2, Q3, Q4; R1= furyl, thienyl, pyridyl, indolyl, biphenyl, (un)substituted phenyl; R13 = C3-4 branched alkyl, C5-6 branched alkenyl, C5-7 cycloalkyl, groups defined in R1; R2 = H, C1-6 alkyl; R3 = each (un)substituted Ph, biphenyl, naphthyl, pyridyl, benzhydryl, thienyl, or furyl; Y = (CH2)l (wherein l = an integer from 1 to 3), or cyclohexane-1,2-diyl; Z = O, S, NH, C1-C3 alkyl-NH, (CH2)n (wherein n =0, 1,2); m = 2,3; R4 = furyl, thienyl, pyridyl, indolyl, biphenyl, (un)substituted phenyl; R5 = thienyl, biphenyl, (un)substituted phenyl] in a mammal. These compds. I are substance P receptor antagonists (no data). The above CNS and other disorders or conditions include sleep disorders, autism, pervasive development disorder, rheumatoid arthritis, osteoarthritis, fibromyalgia, human immunodeficiency virus (HIV) infections, dissociative disorders such as body dysmorphic disorders, eating disorder such as anorexia and bulimia, **ulcerative colitis**, Crohn's disease, irritable bowel syndrome, functional abdominal pain, chronic fatigue syndrome, sudden infant death syndrome (SIDS), overactive bladder, chronic cystitis, chemotherapy induced cystitis, cough, angiotensin converting enzyme (ACE) induced cough, itch, hiccups, premenstrual syndrome, premenstrual dysphoric disorder, schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, schizophreniform disorder, and amenorrheic disorders such as dysmenorrhea. They also include obesity, epilepsy, movement disorders such as primary movement disorders, spasticities, Scott's syndrome, Tourette's syndrome, palsys, amyolateral sclerosis (ALS), akinetic-rigid disorders, akinesias, dyskinesias, restless leg syndrome and movement disorders associated with Parkinson's disease or Huntington's disease, mastalgia syndromes, motion sickness, immune dysfunctions, generalized anxiety disorder, panic disorder, phobias including social phobia, agoraphobia, and specific phobias, obsessive-compulsive disorder, posttraumatic stress disorder; depression including major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression and dysthymia, cyclothymia, bipolar disorder, neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrhythmias including arrhythmias secondary to gastrointestinal disturbances, addiction disorders involving addictions to behaviors, HIV-1 associated dementia, AIDS dementia complex, HIV encephalopathy, HIV related neuralgias, AIDS related neuralgias, epilepsy, and attention deficit hyperactivity disorder in a mammal. Thus, reductive alkylation of 2-diphenylmethyl-1-azabicyclo[2.2.2]octan-3-amine by 2-(difluoromethoxy)benzaldehyde using sodium cyanoborohydride in MeOH at room temperature for 30 h gave 2-(Diphenylmethyl)-N-[(2-difluoromethoxy)phenyl]methyl-1-azabicyclo[2.2.2]octan-3-amine.

IC ICM A61K031-445
ICS A61K031-435

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT Cough
(**angiotensin converting** enzyme-induced; preparation of fluoroalkoxybenzylamino derivs. of nitrogen containing heterocycles as substance P receptor **antagonists** as therapeutic agents)

IT **Inflammation**
Intestine, disease
(**ulcerative colitis**; preparation of fluoroalkoxybenzylamino derivs. of nitrogen containing heterocycles as

substance P receptor antagonists as therapeutic agents)
IT 9015-82-1, **Angiotensin converting** enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cough induced by; preparation of fluoroalkoxybenzylamino derivs. of nitrogen containing heterocycles as substance P receptor **antagonists** as therapeutic agents)

L67 ANSWER 29 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:868260 HCAPLUS
DOCUMENT NUMBER: 136:627
TITLE: Combinations of enzyme inhibitor-containing preparations and the use in inhibition of mononuclear cells and T-cells and treatment of immune conditions
INVENTOR(S): Ansorge, Siegfried; Arndt, Marco; Buehling, Frank; Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk
PATENT ASSIGNEE(S): Institut fuer Medizintechnologie Magdeburg G.m.b.H. IMTM, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089569	A1	20011129	WO 2001-EP5887	20010522 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10025464	A1	20011206	DE 2000-10025464	20000523 <--
CA 2410305	AA	20021122	CA 2001-2410305	20010522 <--
EP 1289559	A1	20030312	EP 2001-945184	20010522 <--
EP 1289559	B1	20050727		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003534293	T2	20031118	JP 2001-585811	20010522 <--
AT 300313	E	20050815	AT 2001-945184	20010522
US 2005014699	A1	20050120	US 2004-296102	20040326

PRIORITY APPLN. INFO.:		
DE 2000-10025464	A	20000523
WO 2001-EP5887	W	20010522

AB A method is disclosed which permits, owing to the simultaneous and joint **inhibition** of the enzyme activities of (1) alanyl-aminopeptidase and dipeptidyl-peptidase IV, (2) dipeptidyl-peptidase IV and **angiotensin-converting** enzyme, (3) dipeptidyl-peptidase IV and prolyl-oligopeptidase, and (4) dipeptidyl-peptidase IV and X-Pro-aminopeptidase, the **inhibition** of DNA synthesis and thus the proliferation of mononuclear cells and T cells to an extent which cannot be obtained by individual application of the enzyme **inhibitors**, even when used in higher doses. Although the above-mentioned inhibitors influence the same process, namely DNA synthesis and thus the proliferation of immune cells, this effect is not complete and not long-lasting when the inhibitors are used individually.

The functional overlapping of enzymic activities results, as is supported by exptl. data, in an additive/superadditive inhibitory effect on DNA synthesis and the proliferation resulting from the simultaneous inhibition of a plurality of the above enzymes. The invention shows that the simultaneous application of inhibitors of the above enzymes or of corresponding prepns. and forms of administration is suitable for the therapy of autoimmune diseases and chronic diseases with an inflammatory genesis, as well as for the treatment of post-transplant rejection episodes.

IC ICM A61K045-06
ICS A61P037-06; A61P035-00; A61K038-55; A61K038-55

CC 1-7 (Pharmacology)

ST peptidase **ACE inhibitor** combination immune disorder; mononuclear cell antiproliferative peptidase **ACE inhibitor** combination; T cell antiproliferative peptidase **ACE inhibitor** combination; autoimmune disease peptidase **ACE inhibitor** combination; transplant rejection peptidase **ACE inhibitor** combination

IT Inflammation
Intestine, disease
(**colitis**, **colitis ulcerosa**; enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

IT 9015-82-1, **Angiotensin-converting** enzyme 9054-63-1, Alanyl aminopeptidase 37288-66-7, Aminopeptidase P 54249-88-6, Dipeptidylpeptidase IV 72162-84-6, Prolyl oligopeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzyme **inhibitor** combinations for **inhibition** of mononuclear cells and T-cells and treatment of immune conditions)

IT 72-18-4D, L-Valine, amidated 73-22-3D, L-Tryptophan, amidated 73-32-5D, L-Isoleucine, amidated 147-85-3D, L-Proline, amidated 2577-48-2 3557-90-2D, amidated 13434-13-4, Actinonin 41721-00-0 54164-07-7 56384-04-4 62023-67-0 **62571-86-2**, Captopril 65921-40-6 **75847-73-3**, Enalapril **76547-98-3**, Lisinopril **88768-40-5**, Cilazapril 88795-32-8 99429-59-1 123652-87-9, Probestin 129085-76-3, Leuhistin 135219-43-1, Poststatin 136259-18-2 136259-19-3 136259-20-6 136259-21-7 136259-22-8 136259-23-9 137563-63-4, Eurystatin A 137563-64-5, Eurystatin B 142880-55-5 148152-02-7 160470-73-5, Apstatin 184360-42-7 187402-73-9, Phebestin 192821-27-5 251571-76-3 252860-55-2 252860-56-3 252860-57-4 252860-58-5 327623-45-0 327983-79-9 376346-22-4 376346-23-5 376346-24-6 376346-25-7 376346-26-8 376346-27-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

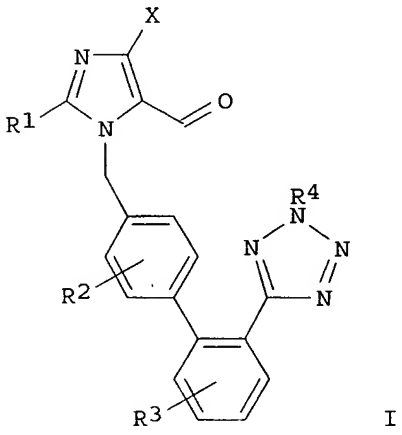
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 30 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:816391 HCAPLUS
DOCUMENT NUMBER: 135:339245
TITLE: Novel tetrazol-biphenyl compounds for the treatment of inflammatory and cardiovascular diseases
INVENTOR(S): Forssmann, Wolf-Georg; Drexler, Helmut; Walden, Michael; Schieffer, Bernhard; Schmidt, Boris
PATENT ASSIGNEE(S): IPF Pharmaceuticals G.m.b.H., Germany
SOURCE: PCT Int. Appl., 11 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082858	A2	20011108	WO 2001-EP5043	20010504 <--
WO 2001082858	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067404	A5	20011112	AU 2001-67404	20010504 <--
PRIORITY APPLN. INFO.:			DE 2000-10021615 A	20000504
			WO 2001-EP5043 W	20010504

OTHER SOURCE(S): MARPAT 135:339245
GI



I

AB The invention concerns a compound having structural formula (I), wherein R1 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Butyl; X = halogen or OH; R2 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu, halogen or OH; R3 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu, halogen or OH; R4 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu or is a metal radical, especially an alkali cation. 2-Butyl-4-chloro-1-[(2'-tetrazol-5-yl)biphenyl-4-yl]methyl-5-(oxomethylene)imidazole can be obtained by the catalytic oxidation of losartan with ruthenium chloride.

IC ICM A61K
CC 1-7 (Pharmacology)
Section cross-reference(s): 28, 63

ST tetrazol biphenyl deriv antiinflammatory cardiovascular agent **ACE inhibitor**

IT **Intestine, disease**
(Crohn's; tetrazol-biphenyl compds. for treatment of **inflammatory** and cardiovascular diseases)

IT Alzheimer's disease
Analgesics
Anti-inflammatory agents
Anticoagulants
Antihypertensives
Antipyretics
Antirheumatic agents
Arthritis
Cardiovascular agents
Celiac disease
Dysmenorrhea
Gout
Osteoarthritis
(tetrazol-biphenyl compds. for treatment of inflammatory and cardiovascular diseases)

IT **Intestine, disease**
(**ulcerative colitis**; tetrazol-biphenyl compds. for treatment of **inflammatory** and cardiovascular diseases)

IT 9015-82-1, **ACE**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitors** of; tetrazol-biphenyl compds. for treatment of inflammatory and cardiovascular diseases)

L67 ANSWER 31 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:703740 HCAPLUS
DOCUMENT NUMBER: 135:251986
TITLE: Methods for treating fibroproliferative diseases with antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides
INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 6,025,151.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294350	B1	20010925	US 1999-433621	19991102 <--
US 5985592	A	19991116	US 1997-870096	19970605 <--
US 6025151	A	20000215	US 1998-92317	19980605 <--
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102 <--
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1997-870096 A2 19970605
US 1998-92317 A2 19980605
US 1999-433621 A1 19991102

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amount of a compound effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional derivative or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compound is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

IC ICM C12Q001-02
ICS C12Q001-00; C12Q001-50

INCL 435029000

CC 1-12 (Pharmacology)
Section cross-reference(s): 9, 63

IT **Intestine, disease**
(**inflammatory**; antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 54-85-3D, Isoniazid, conjugated 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline, derivs. and metabolites 6493-06-7, 1H-Purine-2,6-dione, 3,7-dihydro-1-(5-hydroxyhexyl)-3,7-dimethyl- 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone **62571-86-2**, Captopril **75847-73-3**, Enalapril 80288-49-9, Furafylline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 9015-82-1, **Angiotensin converting** enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 32 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:452872 HCAPLUS
DOCUMENT NUMBER: 135:56494
TITLE: Methods for treating and preventing damage to mucosal tissue using angiotensinogen, angiotensin I, AI analogs, AI fragments and analogs, angiotensin II, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists
INVENTOR(S): Rodgers, Kathleen E.; Dizerega, Gere S.

PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043761	A2	20010621	WO 2000-US32141	20001127 <--
WO 2001043761	A3	20020307		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393755	AA	20010621	CA 2000-2393755	20001127 <--
AU 2001017931	A5	20010625	AU 2001-17931	20001127 <--
EP 1239867	A2	20020918	EP 2000-980704	20001127 <--
EP 1239867	B1	20050126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517019	T2	20030520	JP 2001-544898	20001127 <--
US 6821953	B1	20041123	US 2000-723257	20001127 <--
AT 287724	E	20050215	AT 2000-980704	20001127
US 2005004036	A1	20050106	US 2004-875155	20040623

PRIORITY APPLN. INFO.:		
US 1999-171249P	P	19991216
US 2000-213224P	P	20000619
US 2000-723257	A1	20001127
WO 2000-US32141	W	20001127

OTHER SOURCE(S): MARPAT 135:56494

AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing damage to mucosal tissue by administering an effective amount of angiotensinogen, angiotensin I (AI), AI analogs, AI fragments and analogs thereof, angiotensin II (AII), AII analogs, AII fragments or analogs thereof or AII AT2 type 2 receptor agonists to the subject. Administration of anti-inflammatory drugs, **angiotensin converting** enzyme **inhibitors**, anti-infectives, growth factors, and/or antihistamines in combination with the above compns. is also claimed.

IC ICM A61K038-00
CC 2-10 (Mammalian Hormones)
IT **Intestine, disease**
(**ulcerative colitis**, non-specific inflammations; methods for treating and preventing damage to mucosal tissue using angiotensinogen, AI, AI analogs, AI fragments and analogs, AII, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists)
IT 9015-82-1, **Angiotensin converting** enzyme
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitor**; methods for treating and preventing damage to mucosal tissue using angiotensinogen, AI, AI analogs, AI fragments and analogs, AII, AII analogs, AII fragments or analogs or AII AT2 type 2

receptor agonists)

L67 ANSWER 33 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:427871 HCAPLUS
DOCUMENT NUMBER: 135:266468
TITLE: Fish oil - a potential therapy for inflammatory atherosclerosis
AUTHOR(S): Saldeen, Tom; Mehta, Jay L.
CORPORATE SOURCE: Department of Surgical Sciences, University of Uppsala, Uppsala, 752 37, Swed.
SOURCE: Inflammatory and Infectious Basis of Atherosclerosis (2001), 243-257. Editor(s): Mehta, Jay L. Birkhaeuser Verlag: Basel, Switz.
CODEN: 69BJTK
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 70 refs. Inflammation plays an important role in both the initiation of atherosclerosis and the development of atherothrombotic events. An anti-inflammatory effect of n-3 fatty acids in fish oil was suggested by epidemiol. studies which show that Greenland Eskimos, who consume large quantities of fish oils rich in long-chain n-3 fatty acids, have a very low incidence not only of atherosclerosis and coronary artery disease but also of inflammatory and autoimmune disorders such as rheumatoid arthritis, psoriasis, asthma, **inflammatory bowel** disease, type I diabetes mellitus, thyrotoxicosis and multiple sclerosis. Fifteen large studies enrolling more than 60,000 subjects have shown a decreased mortality in CAD as well as in total mortality of about 20-30% after intake of fish oil, fatty fish or n-3 fatty acids. In a randomized controlled trial on the effect of intake of fatty fish or natural fish oil, 2033 men who had recovered from myocardial infarction were studied for two years. The fish/fish oil group showed a 29% reduction in two year all-cause mortality. In another study enrolling 11,324 patients surviving a recent myocardial infarction, intake of 1 g daily of n-3 fatty acids in 2,836 patients for 3.5 yr resulted in a 20% decrease in total deaths, a 30% decrease in cardiovascular deaths and a 45% decrease in sudden deaths. Interestingly, these patients already had conventional treatment with aspirin, beta-**blockers** and **angiotensin converting** enzyme **inhibitors** and were already exposed to a healthy Mediterranean diet. Thus, there seems to be no doubt that fish oil has a beneficial effect on CAD. Stable fish oil has many interesting effects suggesting a major role for this oil as a potential therapy for inflammatory atherosclerosis.
CC 1-0 (Pharmacology)
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 34 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:338333 HCAPLUS
DOCUMENT NUMBER: 134:357558
TITLE: Methods for treating fibroproliferative diseases
INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102 <--
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6294350	B1	20010925	US 1999-433621	19991102 <--
PRIORITY APPLN. INFO.:			US 1999-433621	A1 19991102
			US 1997-870096	A2 19970605
			US 1998-92317	A2 19980605

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization ofc-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amount of a compound effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional derivative or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compound is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

IC ICM A61K031-00
ICS A61K031-522; A61K045-00; A61K045-06; A61K048-00; C12Q001-48; G01N033-58; A61P019-04; A61P035-00; A61P037-00; A61P025-28; A61P043-00; A61P033-06; A61P031-12; A61P039-00; A61P035-02; A61P001-00; A61P011-00; A61P013-12; A61P009-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 8, 15

IT **Intestine, disease**
(**inflammatory**; antisense oligonucleotide prepns. for treating fibroproliferative diseases)

IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-06-7 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone **62571-86-2**, Captopril **75847-73-3**, Enalapril 80288-49-9, Furafylline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense oligonucleotide prepns. for treating fibroproliferative diseases)

IT 9015-82-1, **Angiotensin converting** enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antisense oligonucleotide prepns. for treating fibroproliferative diseases)

L67 ANSWER 35 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:790293 HCAPLUS
DOCUMENT NUMBER: 133:344615
TITLE: ACE-2 inhibiting compounds, their preparation, pharmaceutical compositions containing them, and their therapeutic use
INVENTOR(S): Acton, Susan L.; Ocain, Timothy D.; Gould, Alexandra E.; Dales, Natalie A.; Guan, Bing; Brown, James A.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066104	A2	20001109	WO 2000-US11550	20000428 <--
WO 2000066104	A3	20010628		
WO 2000066104	C2	20020829		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2372387	AA	20001109	CA 2000-2372387	20000428 <--
EP 1183019	A2	20020306	EP 2000-926478	20000428 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103094	T2	20020321	TR 2001-200103094	20000428 <--
BR 2000010166	A	20020604	BR 2000-10166	20000428 <--
JP 2002543120	T2	20021217	JP 2000-614989	20000428 <--
US 6632830	B1	20031014	US 2000-561759	20000428 <--
NO 2001005274	A	20011228	NO 2001-5274	20011029 <--
ZA 2001009378	A	20021114	ZA 2001-9378	20011114 <--

PRIORITY APPLN. INFO.:

US 1999-132034P	P	19990430
US 1999-171052P	P	19991216
WO 2000-US11550	W	20000428

OTHER SOURCE(S): MARPAT 133:344615

AB ACE-2 inhibiting compds. are disclosed. Methods of using the compds. and pharmaceutical compns. containing the compds. are also claimed. The compds. of the invention are useful for treating e.g. blood pressure-related diseases. Compound preparation is described.

IC ICM A61K031-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 34, 63
ST ACE2 inhibitor prepn therapeutic; blood pressure disease ACE2 inhibitor; **angiotensin converting** enzyme 2 **inhibitor** therapeutic
IT **Intestine, disease**
(**inflammatory**; ACE-2 inhibitor preparation, pharmaceutical compns., and therapeutic use)
IT 1407-47-2, Angiotensin 9015-82-1, **Angiotensin-**

converting enzyme 9041-90-1, Angiotensin I 11075-17-5, Carboxypeptidase A 23827-88-5, 2-8-Bradykinin 23828-06-0, 2-7-Bradykinin 55508-42-4, Neurotensin(1-13) 63529-99-7, Neurotensin(1-12) 189696-01-3 305336-82-7 305336-84-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ACE-2 **inhibitor** preparation, pharmaceutical compns., and therapeutic use)

L67 ANSWER 36 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688272 HCAPLUS
DOCUMENT NUMBER: 133:280563
TITLE: Human antibodies that bind human IL-12 and methods for producing
INVENTOR(S): Salfeld, Jochen G.; Roguska, Michael; Paskind, Michael; Banerjee, Subhashis; Tracey, Daniel E.; White, Michael; Kaymakcalan, Zehra; Labkovsky, Boris; Sakorafas, Paul; Friedrich, Stuart; Myles, Angela; Veldman, Geertruida M.; Venturini, Amy; Warne, Nicholas W.; Widom, Angela; Elvin, John G.; Duncan, Alexander R.; Derbyshire, Elaine J.; Carmen, Sara; Smith, Stephen; Holtet, Thor Las; Du, Fou Sarah L.
PATENT ASSIGNEE(S): Basf A.-G., Germany; Genetics Institute Inc.; et al.
SOURCE: PCT Int. Appl., 377 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000056772	A1	20000928	WO 2000-US7946		20000324 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2365281	AA	20000928	CA 2000-2365281		20000324 <--
NZ 513945	A	20010928	NZ 2000-513945		20000324 <--
BR 2000009323	A	20020108	BR 2000-9323		20000324 <--
EP 1175446	A1	20020130	EP 2000-918396		20000324 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200102715	T2	20020923	TR 2001-200102715		20000324 <--
JP 2002542770	T2	20021217	JP 2000-606632		20000324 <--
US 6914128	B1	20050705	US 2000-534717		20000324
ZA 2001007774	A	20021220	ZA 2001-7774		20010920 <--
NO 2001004605	A	20011126	NO 2001-4605		20010921 <--
BG 106027	A	20020628	BG 2001-106027		20011018 <--
NZ 529571	A	20031219	NZ 2003-529571		20031117 <--
US 2005004354	A1	20050106	US 2004-884830		20040701
PRIORITY APPLN. INFO.:			US 1999-126603P	P	19990325
			US 2000-534717	A3	20000324
			WO 2000-US7946	W	20000324

AB Human antibodies, preferably recombinant human antibodies, that specifically bind to human interleukin-12 (hIL-12) are disclosed. Preferred antibodies have high affinity for hIL-12 and neutralize hIL-12 activity in vitro and in vivo . An antibody of the invention can be a full-length antibody or an antigen-binding portion thereof. The antibodies, or antibody portions, of the invention are useful for detecting hIL-12 and for inhibiting hIL-12 activity, e.g., in a human subject suffering from a disorder in which hIL-12 activity is detrimental. Nucleic acids, vectors and host cells for expressing the recombinant human antibodies of the invention, and methods of synthesizing the recombinant human antibodies, are also encompassed by the invention.

IC ICM C07K016-24
ICS C12N015-13; C12N015-63; C12N005-10; C07K016-00; A61K039-395; G01N033-577; C12P021-08; A61P043-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

IT **Intestine, disease**
(Crohn's; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT **Intestine, disease**
(**inflammatory**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT **Intestine, disease**
(**ulcerative colitis**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT 9004-06-2, Elastase 9015-82-1, **Angiotensin converting** enzyme 9025-82-5, Phosphodiesterase 9029-60-1, Lipoxygenase 122191-40-6, Interleukin 1β converting enzyme 151769-16-3, TNFα converting enzyme
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitors**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and inflammatory diseases)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 37 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:534969 HCAPLUS
DOCUMENT NUMBER: 133:140262
TITLE: Slow-release pharmaceutical compositions
INVENTOR(S): Huber, Gerald; Gruber, Peter
PATENT ASSIGNEE(S): Losan Pharma G.m.b.H., Germany
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044353	A1	20000803	WO 1999-IB180	19990129 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2360655	AA	20000803	CA 1999-2360655	19990129 <--
AU 9919808	A1	20000818	AU 1999-19808	19990129 <--
AU 764469	B2	20030821		
EP 1146862	A1	20011024	EP 1999-900623	19990129 <--
EP 1146862	B1	20030423		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

BR 9916972	A	20011106	BR 1999-16972	19990129 <--
JP 2002535353	T2	20021022	JP 2000-595657	19990129 <--
AT 238040	E	20030515	AT 1999-900623	19990129 <--
NZ 513037	A	20030530	NZ 1999-513037	19990129 <--
PT 1146862	T	20030930	PT 1999-900623	19990129 <--
ES 2197600	T3	20040101	ES 1999-900623	19990129 <--
NO 2001003336	A	20010925	NO 2001-3336	20010705 <--
US 6962717	B1	20051108	US 2001-890104	20011016
PRIORITY APPLN. INFO.:			EP 1999-900623 A	19990129
			WO 1999-IB180 A	19990129

AB A pharmaceutical composition for the slow release of an active agent in the gastrointestinal tract comprises multiple particles which contain an active agent and which are coated with a material that is insol. in gastrointestinal juice. The particles have a core consisting of a homogeneous mixture of pharmaceutical active agent and a polymer which is insol. in gastrointestinal juice, with a maximum average inner pore diameter of 35 μm. The composition enables an efficient release which is independent of pH, even with comparatively small quantities of polymer, and has good stability during storage. Thus, a mixture of 5-aminosalicylic acid (I) 175, Eudragit RS30D 29.167, and tri-Et citrate 1.750 kg was granulated with 7.65 kg H2O, dried at 50-90°, compacted, coated with a suspension containing Eudragit NE40D 20.869, talc 4.435, 33% simethicone antifoam emulsion 0.509, and H2O 20.867 kg, and 198.450 kg of the coated granules (maximum size 1000 μm) were mixed with microcryst. cellulose 50.421, Kollidon K90 3.129, and Kollidon CL 14.000 kg in a cyclone granulator and compressed into 760-mg tablets each containing 500.00 mg I. These tablets released 24.9 and 82.5% of their I content after 30 and 240 min, resp., at pH 1.2.

IC ICM A61K009-16
ICS A61K009-50; A61K009-00; A61K009-20; A61K009-48

CC 63-6 (Pharmaceuticals)

IT **Intestine, disease**
(**ulcerative colitis**; slow-release pharmaceutical compns.)

IT 52-26-6, Morphine hydrochloride 57-27-2, Morphine, biological studies 89-57-6, 5-Aminosalicylic acid 26787-78-0, Amoxicillin 27203-92-5, Tramadol 36282-47-0, Tramadol hydrochloride 51333-22-3, Budesonide 58001-44-8, Clavulanic acid 59277-89-3, Acyclovir 66357-35-5, Ranitidine 73590-58-6, Omeprazole **75847-73-3**, Enalapril 76824-35-6, Famotidine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 88150-42-9, Amlodipine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(slow-release pharmaceutical compns.)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 38 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:144772 HCAPLUS
DOCUMENT NUMBER: 132:189689
TITLE: Bioreductive conjugates for drug targeting
INVENTOR(S): Adams, Ged; Blake, David; Naughton, Declan; Stratford, Ian
PATENT ASSIGNEE(S): Theramark Limited, UK; Adams, Margaret
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000010610	A2	20000302	WO 1999-GB2606		19990819 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9954296	A1	20000314	AU 1999-54296		19990819 <--
PRIORITY APPLN. INFO.:			GB 1998-18027	A	19980819
			GB 1998-18156	A	19980820
			WO 1999-GB2606	W	19990819

OTHER SOURCE(S): MARPAT 132:189689

AB The use of a bioreductive conjugate comprised of a noncytotoxic bioreductive moiety having linked thereto at least one therapeutic agent, and salts thereof, is disclosed for the healing of wounds and the treatment of fibrotic disorders, **ulcerative colitis**, **inflammatory bowel** disease, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers dementia, oncol., AIDS, rheumatoid arthritis, diabetes, and ischemia. Various specific conjugates for treating these conditions are also disclosed.

IC ICM A61K047-48
CC 1-12 (Pharmacology)
IT **Intestine, disease**
(**inflammatory**; bioreductive conjugates for drug targeting)
IT **Stomach, disease**
(**ulcer**; bioreductive conjugates for drug targeting)
IT **Intestine, disease**
(**ulcerative colitis**; bioreductive conjugates for drug targeting)
IT 50-06-6D, Phenobarbitone, conjugates, biological studies 50-24-8D, Prednisolone, conjugates 50-78-2D, Aspirin, conjugates 52-53-9D, Verapamil, conjugates 52-67-5D, Penicillamine, conjugates 53-86-1D, Indomethacin, conjugates 57-41-0D, Phenytoin, conjugates 58-32-2D, Dipyridamole, conjugates 59-05-2D, Methotrexate, conjugates 66-97-7D, Psoralen, conjugates 89-57-6D, Mesalazine, conjugates 89-57-6D, 5-Aminosalicylic acid, derivs., conjugates 118-42-3D, Hydroxychloroquine, conjugates 305-03-3D, Chlorambucil, conjugates 443-48-1D, Metronidazole, conjugates 446-86-6D, Azathioprine, conjugates 599-79-1D, Sulfasalazine, conjugates 1069-66-5D, Sodium valproate,

conjugates 1406-16-2D, Vitamin D, analogs, conjugates 6556-11-2D, Inositol nicotinate, conjugates 12244-57-4D, Myochrysine, conjugates 15307-86-5D, Diclofenac, conjugates 15687-27-1D, Ibuprofen, conjugates 21829-25-4D, Niphedipine, conjugates 22204-53-1D, Naproxen, conjugates 26171-23-3D, Tolmetin, conjugates 29679-58-1D, Fenoprofen, conjugates 38194-50-2D, Sulindac, conjugates 51234-28-7D, Benoxaprofen, conjugates 56180-94-0D, Acarbose, conjugates 59865-13-3D, Cyclosporin A, conjugates **62571-86-2D**, Captopril, conjugates 67763-97-7D, Insulin-like growth factor II, conjugates 73590-58-6D, Omeprazole, conjugates 79217-60-0D, Cyclosporin, derivs., conjugates **87333-19-5D**, Ramipril, conjugates **87679-37-6D**, Trandolapril, conjugates 97240-79-4D, Topiramate, conjugates 103577-45-3D, Lansoprazole, conjugates 113194-81-3, TMK 209 117976-89-3D, Rabeprazole, conjugates 259876-40-9, TMK 210 259876-41-0, TMK 207
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioreductive conjugates for drug targeting)

IT 9015-82-1, **Angiotensin-converting** enzyme 9025-82-5, Phosphodiesterase 9036-21-9, Phosphodiesterase IV 9055-65-6, Prostaglandin synthetase 9068-52-4, Phosphodiesterase V 81669-70-7, Metalloprotease 99676-46-7, Kexin 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; bioreductive conjugates for drug targeting)

L67 ANSWER 39 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:573330 HCAPLUS
DOCUMENT NUMBER: 132:91438
TITLE: Lipid peroxidation and tissue damage
AUTHOR(S): Mylonas, Chrisostomos; Kouretas, Demetrios
CORPORATE SOURCE: Department of Pharmacology, University of Leeds, Leeds, LS2 9JT, UK
SOURCE: In Vivo (**1999**), 13(3), 295-309
CODEN: IVIVE4; ISSN: 0258-851X
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Review with 56 refs. In recent years it has become apparent that the oxidation of lipids, or lipid peroxidn., is a crucial step in the pathogenesis of several disease states in adult and infant patients. Lipid peroxidn. is a process generated naturally in small amts. in the body, mainly by the effect of several reactive oxygen species (hydroxyl radical, hydrogen peroxide etc.). It can also be generated by the action of several phagocytes. These reactive oxygen species readily attack the polyunsatd. fatty acids of the fatty acid membrane, initiating a self-propagating chain reaction. The destruction of membrane lipids and the end-products of such lipid peroxidn. reactions are especially dangerous for the viability of cells, even tissues. Enzymic (catalase, superoxide dismutase) and nonenzymic (vitamins A and E) natural antioxidant defense mechanisms exist; however, these mechanisms may be overcome, causing lipid peroxidn. to take place. Since lipid peroxidn. is a self-propagating chain-reaction, the initial oxidation of only a few lipid mols. can result in significant tissue damage. Despite extensive research in the field of lipid peroxidn. it has not yet been precisely determined if it is the cause or an effect of several pathol. conditions. Lipid peroxidn. has been implicated in disease states such as atherosclerosis, **inflammatory bowel** disease, retinopathy of prematurity, bronchopulmonary dysplasia, asthma, Parkinson's disease, kidney damage, preeclampsia and others.

CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
IT **Intestine, disease**
(**inflammatory**; lipid peroxidn. and its relation to tissue damage in different pathol. states)
IT 73-31-4, Melatonin **62571-86-2**, Captopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant; lipid peroxidn. and its relation to tissue damage in different pathol. states)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 40 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:453581 HCAPLUS
DOCUMENT NUMBER: 129:215128
TITLE: The pathogenetic role of endogenous angiotensin II in stress ulcer in obstructive jaundice rats
AUTHOR(S): Mou, Dongcheng; Zhu, Xueguang; Xu, Wei; Du, Ruyu
CORPORATE SOURCE: Department of Surgery, Sichuan People's Hospital, Chengdu, 610072, Peop. Rep. China
SOURCE: Chinese Medical Journal (Beijing, English Edition) (**1998**), 111(4), 309-312
CODEN: CMJODS; ISSN: 0366-6999
PUBLISHER: Chinese Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim was to investigate the pathogenetic role of endogenous **angiotensin** II (Ang II) in the mechanism of stress ulcer in obstructive jaundice rats and to detect the effect of **angiotensin converting** enzyme **inhibitor** (ACEI) on stress ulcer in obstructive jaundice rats. After common bile duct ligation (CBDL) in Wistar rats, the content of plasma and gastric mucosal Ang II, gastric mucosal blood flow (GMBF) and gastric mucosal damage were measured, and the relation among them was analyzed. The plasma Ang II contents increased much more significantly at 1, 3, 7 and 14 days following CBDL than those in non-CBDL rats. Within 120 min following cold-restraint stress, plasma and gastric mucosal Ang II contents were elevated, GMBF decreased, and ulcer index and gastric mucosal damage increased more significantly than those in non-cold-restraint stress rats. Administration of an ACEI, enalapril, to CBDL rats (5 mg·kg-1·day-1, orally for two days) before stress reduced both the plasma and gastric mucosal Ang II levels, inhibited the decrease of GMBF and decreased ulcer index and gastric mucosal damage. The endogenous Ang II plays a significant pathogenetic role in the development of stress ulcer in obstructive jaundice rats, and ACEI may prevent stress ulcer.
CC 14-7 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 2
ST angiotensin II stress ulcer obstructive jaundice; **ACE inhibitor** stress ulcer angiotensin II
IT Blood plasma
(**angiotensin** II; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)
IT Stress, animal
(cold-restraint; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)
IT Circulation

(gastric mucosal; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT Stomach
(mucosa, **angiotensin** II and blood flow; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT Jaundice
(obstructive; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT Antiulcer agents
(pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT Stress, animal
(restraint, cold-restraint stress; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT **Stomach, disease**
(**ulcer**, stress; pathogenetic role of endogenous **angiotensin** II in stress **ulcer** in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT 9015-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT 9015-82-1, **Angiotensin converting** enzyme
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT 11128-99-7, **Angiotensin** II
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

IT **75847-73-3**, Enalapril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pathogenetic role of endogenous **angiotensin** II in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting** enzyme **inhibitor**)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 41 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:138222 HCAPLUS
DOCUMENT NUMBER: 126:229452

TITLE: The rationale for peptide drug delivery to the colon and the potential of polymeric carriers as effective tools

AUTHOR(S): Rubinstein, Abraham; Tirosh, Boaz; Baluom, Muhammad; Nassar, Taher; David, Ayelet; Radai, Raphael; Gliko-Kabir, Irit; Friedman, Michael

CORPORATE SOURCE: The Hebrew University of Jerusalem, School of Pharmacy, The David R. Bloom Center of Pharmacy, P.O. Box 12065, Jerusalem, Israel

SOURCE: Journal of Controlled Release (**1997**), 46(1,2), 59-73
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 111 refs. The explicit use of colon-specific drug delivery systems is for the local treatment of colon diseases such as **ulcerative colitis**. Some efficient therapeutic systems, primarily prodrugs and polymeric carriers of salicylate derivs., have been developed and commercialized during the past 20 yr. Speculating that the colon is a superior organ for peptide drug absorption after oral ingestion, many studies indicate that colon-specific drug carriers may potentially be used for the delivery of peptide drugs to that organ. This notion stems from the assumption that the overall proteolytic activity in the colon is lower than and different from the proteolytic activity in the small intestine, e.g., the degradation rate of albumin, azo-albumin casein, azo-casein and collagen in human ileal effluent was faster than the degradation rate in fecal slurries. Other studies, in which the degradation rates of insulin and insulin B-chain in the small and large intestine of the guinea pig were compared, showed higher degradation rates in the small intestine. It is noteworthy, however, that a peptide drug may stay much longer (up to 10-fold longer) in the large intestine. Thus, even if the enzymic activity is lower, the drug is exposed longer to proteolytic activity. Yet, if the drug is properly protected or formulated with absorption enhancers, the prolonged residence time may increase drug absorption from the large intestine. Thus, prolonged drug blood levels of the **ACE inhibitors** benazepril and captopril have been demonstrated in a number of studies after colonic administration to rats and dogs. A possible explanation for the 'flat' pharmacokinetic profiles obtained may be the 'closed compartment conditions' existing in the colon resulting from the extremely slow propulsive movement of digesta in that organ. These almost stationary conditions may also benefit the performance of functional adjuvants, such as absorption enhancers or peptidase inhibitors, because their dilution rate with the luminal contents of the colon is low. For the purpose of colon-specific drug delivery a variety of polymers has been developed, including acrylic polymers modified with azo crosslinkers and saccharide polymers. Both kinds have been tested in vitro and in animal studies for their ability to be degraded specifically by typical enzymes of the colon. In addition, swellable polymers were utilized in new pulsatile and delayed-release colonic delivery systems after being protected with enteric coating polymers. To secure peptide drugs in the GI tract, especially in the colon, the use of cross-linked acrylic acid derivs. such as polycarbophil and Carbopol 934 has also been suggested. New biodegradable polymers and polymers with controllable swelling properties can be used for the specific delivery of drugs to the colon. Furthermore, some polymers, by virtue of their intrinsic proteolytic inhibition properties, could be used

to improve the absorption of peptide drugs from colonic delivery systems.
CC 63-0 (Pharmaceuticals)
Section cross-reference(s): 1, 2

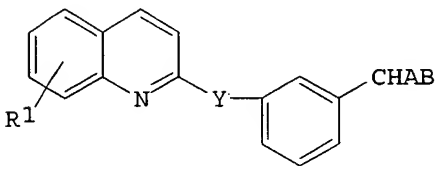
L67 ANSWER 42 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:480039 HCAPLUS
DOCUMENT NUMBER: 121:80039
TITLE: Protective effects of the inhibition of the renin-angiotensin system against gastric mucosal lesions induced by cold-restraint in the rat
AUTHOR(S): Ender, F.; Labancz, T.; Rosivall, L.
CORPORATE SOURCE: Dep. Surg. SCHOPF-MEREI Hosp., SEMMEL WEIS Univ. Med. Sch., BUDAPEST, Hung.
SOURCE: Acta Physiologica Hungarica (**1993**), 81(1), 13-18
CODEN: APHHDU; ISSN: 0231-424X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Expts. were designed to examine whether inhibition of the renin-angiotensin system alters gastric mucosal damage in conscious rats subjected to restraint. Two hours immobilization resulted in an ulcer index of 46 ± 4 (n = 16) which was decreased by converting enzyme inhibitor (MK 422, enalaprilat) doses of 1 and 10 mg·kg-1·h-1 by 50 ± 16 (n = 8) and 66 ± 8% (n = 13), resp. ($p < 0.05$). Gastric blood flow measured by both the 99Tc-labeled frog erythrocytes and 86Rb-clearance methods was low in untreated rats and increased to more than three-fold in **angiotensin converting** enzyme **inhibitor** treated animals. Infusion of saralasin a specific angiotensin II receptor blocker (5 μg·kg-1·h-1, n = 25) also decreased the ulcer index by 40 ± 5% ($p < 0.05$). Thus inhibition of the renin-angiotensin system in conscious cold-restraint rat increased gastric blood flow and reduced mucosal damage. These results suggest that the renin-angiotensin system plays a significant role in the development of exptl. gastric ulcer in the cold-restraint model.
CC 14-7 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
ST stress **stomach ulcer** pathogenesis renin angiotensin; enalaprilat stress **stomach ulcer** inhibition; saralasin stress **stomach ulcer** inhibition
IT Stress, biological
(**stomach ulceration** from, renin-angiotensin system in)
IT Receptors
RL: BIOL (Biological study)
(angiotensin II, in stress-induced **stomach ulceration**)
IT 9015-94-5, Renin, biological studies
RL: BIOL (Biological study)
(-angiotensin system, in stress-induced **stomach ulceration**)
IT 1407-47-2, Angiotensin
RL: BIOL (Biological study)
(-renin system, in stress-induced **stomach ulceration**)
IT 9015-82-1, **Angiotensin converting** enzyme
RL: BIOL (Biological study)
(**inhibition** of, stress-induced **stomach ulceration** prevention by)
IT 11128-99-7, Angiotensin

RL: BIOL (Biological study)
(receptors for, in stress-induced **stomach ulceration**
)
IT 34273-10-4, Saralasin **76420-72-9**, Enalaprilat
RL: BIOL (Biological study)
(stress-induced **stomach ulceration** prevention by)

L67 ANSWER 43 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:656016 HCAPLUS
DOCUMENT NUMBER: 115:256016
TITLE: Preparation of diarylstyrylquinoline diacids as leukotriene antagonists
INVENTOR(S): Young, Robert N.; Gauthier, Jacques Yves; Zamboni, Robert; Belley, Michel L.
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Cote d'Ivoire
SOURCE: Eur. Pat. Appl., 144 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 399818	A1	19901128	EP 1990-305640	19900523 <--
EP 399818	B1	19950816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5104882	A	19920414	US 1990-527236	19900522 <--
CA 2017376	AA	19901124	CA 1990-2017376	19900523 <--
CA 2017376	C	20000718		
NO 9002301	A	19901126	NO 1990-2301	19900523 <--
AU 9055811	A1	19901213	AU 1990-55811	19900523 <--
ZA 9003983	A	19910327	ZA 1990-3983	19900523 <--
JP 03072459	A2	19910327	JP 1990-132754	19900524 <--
JP 07103107	B4	19951108		
US 5204358	A	19930420	US 1992-818598	19920109 <--

PRIORITY APPLN. INFO.:
US 1989-356478 A 19890524
US 1987-125050 B2 19871125
US 1988-275160 B2 19881122
US 1990-527236 A3 19900522
OTHER SOURCE(S): MARPAT 115:256016
GI



I

AB Title compds. I [R1 = 7-Cl, 7-MeO, 6-F3C, 7-F3C, 6-MeSO2, H, 6,7-Cl2; Y = CH:CH, CH2CH2, CH2O, CHMeCH2; A = HO2C(CH2)2S, Me2NCO(CH2)2S, 3-(HO2C)C6H4S, Me3CNHCO(CH2)2S, 4-carboxy-2-pyridyl, [(1-adamantylamino)carbonylethyl]thio, 1-tetrazol-5-ylmethylthio, etc.; B = 2-(HO2C)C6H4CH2CH2, 3-(HO2C)C6H4, 5-carboxy-2-thiophenyl, HO2CCH2CHMe(CH2)2, 6-carboxy-2-pyridyl, 2-(Me3CNHCO)C6H4S,

3-[(1-tetrazol-5-yl)methyl]phenyl, etc.] and their salts, useful as inhibitors of leukotriene biosynthesis, antiasthmatic, antiallergic, antiinflammatory, and cytoprotective agents (no data, assays described), are prepared I may also be used to treat erosive gastritis, **inflammatory bowel** disease, prevention of SRA-release (no data). To a suspension of [(7-chloroquinolin-2-yl)methyl]triphenylphosphonium bromide in THF was added BuLi, the reaction mixture was stirred at -78° and Me 2-[3-[2-(methoxycarbonyl)ethylthio]-3-(3-formylphenyl)propyl]benzoate [preparation from 3-(BrCH2)C6H4CN given] added, the mixture warmed to room temperature to give I [R1 = 7-Cl; Y = CH:CH; A = HO2C(CH2)2S; B = 2-(HO2C)C6H4CH2CH2] (II) as the di-Me ester, which in THF and MeOH was saponified to give II.2Na salt. A capsule, injectable suspension and tablet formulations comprising I are given. Pharmaceutical composition of I may comprise an addnl. active ingredient such as nonsteroidal antiinflammatory drug, peripheral analgesic, cyclooxygenase inhibitor, etc.

IC ICM C07D215-18
ICS C07D215-14; C07D215-20; C07D215-36; C07D401-12; C07D405-12; C07D409-10; A61K031-47

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 9015-82-1, **Angiotensin-converting** enzyme 39391-18-9, Cyclooxygenase 61276-89-9, Thromboxane synthetase
RL: USES (Uses)
(**inhibitors**, leukotriene **antagonists** containing)

L67 ANSWER 44 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:542275 HCAPLUS
DOCUMENT NUMBER: 115:142275
TITLE: Pharmaceutical compositions containing an **angiotensin-converting** enzyme (**ACE) inhibitor** for the treatment of hypermotility diseases of the bowel.
INVENTOR(S): Moore, Luana R. C.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 418582	A2	19910327	EP 1990-116153	19900823 <--
EP 418582	A3	19921007		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2021408	AA	19910301	CA 1990-2021408	19900718 <--
JP 03093720	A2	19910418	JP 1990-222329	19900822 <--

PRIORITY APPLN. INFO.: US 1989-401377 A 19890831

AB Hypermotility diseases of the bowel (irritable bowel syndrome, etc.) are treated with an **ACE inhibitor** (e.g. captopril, fosinopril, ceramapril, enalapril, lisinopril, zofenopril) which may be administered by suppository, enema, or by oral dosage forms that release drug in the colon. Suppository and other formulations are given.

IC ICM A61K031-40
ICS A61K031-675

CC 63-6 (Pharmaceuticals)

ST **angiotensin converting** enzyme **inhibitor** bowel hypermotility; suppository **ACE inhibitor** bowel hypermotility; enalapril bowel hypermotility; captopril bowel hypermotility; zofenopril bowel hypermotility; lisinopril bowel hypermotility; fosinopril bowel hypermotility; ceranapril bowel hypermotility

IT Intestine, disease or disorder
(hypermotility, treatment of, **angiotensin-converting** enzyme **inhibitors** for)

IT Amino acids, biological studies
RL: BIOL (Biological study)
(phosphonate-substituted, as **angiotensin-converting** enzyme **inhibitors**, for bowel hypermotility disease treatment)

IT Intestine, disease or disorder
(Crohn's, treatment of, **angiotensin-converting** enzyme **inhibitor** for)

IT **Diarrhea**
(**chronic**, treatment of, **angiotensin-converting** enzyme **inhibitor** for)

IT Intestine, disease or disorder
(colitis, treatment of, **angiotensin-converting** enzyme **inhibitor** for)

IT Peptides, biological studies
RL: BIOL (Biological study)
(di-, carboxyalkyl, as **angiotensin-converting** enzyme **inhibitors**, for bowel hypermotility disease treatment)

IT Digestive tract
(disease, diabetic, treatment of, **angiotensin-converting** enzyme **inhibitor** for)

IT Digestion, biological
(disorder, hypermotility, treatment of, of bowel, **angiotensin-converting** enzyme **inhibitors** for)

IT Pharmaceutical dosage forms
(enemas, of **angiotensin-converting** enzyme **inhibitor** for bowel hypermotility disease treatment)

IT Carboxylic acids, biological studies
RL: BIOL (Biological study)
(imino, phosphonate-substituted, as **angiotensin-converting** enzyme **inhibitors**, for bowel hypermotility disease treatment)

IT Intestine, disease or disorder
(irritable bowel syndrome, treatment of, **angiotensin-converting** enzyme **inhibitor** for)

IT Peptides, biological studies
RL: BIOL (Biological study)
(phosphino-, as **angiotensin-converting** enzyme **inhibitors**, for bowel hypermotility disease treatment)

IT Pharmaceutical dosage forms
(suppositories, of **angiotensin-converting** enzyme **inhibitor** for bowel hypermotility disease treatment)

IT 147-85-3D, Proline, derivs.
RL: BIOL (Biological study)
(**angiotensin-converting** enzyme **inhibitors**, for bowel hypermotility disease treatment)

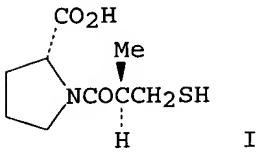
IT **62571-86-2**, Captopril **75847-73-3** **76547-98-3**, Lisinopril 81872-10-8, Zofenopril **98048-97-6**, Fosinopril **111223-26-8**
RL: BIOL (Biological study)
(as **angiotensin-converting** enzyme **inhibitor**

for bowel hypermotility disease treatment)
IT 9015-82-1, **Angiotensin-converting** enzyme
RL: BIOL (Biological study)
(**inhibitors** of, for bowel hypermotility disease treatment)

L67 ANSWER 45 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:161253 HCAPLUS
DOCUMENT NUMBER: 108:161253
TITLE: Effect of kininotropic drugs on ulcerogenesis in rats
AUTHOR(S): Faermark, I. F.; Shvarts, G. Ya.
CORPORATE SOURCE: VNIKhFI, Moscow, USSR
SOURCE: Farmakologiya i Toksikologiya (Moscow) (**1988**), 51(2), 82-4
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The effects of several kininotropic drugs on gastric ulcer development were studied in rats given ulcerogenic doses of histamine, EtOH, reserpine, and Na diclofenac. Antiulcer activities of the kininogenesis inhibitor trasylol and activator cellulose sulfate, the kinin antagonist parmidine, and the kininase inhibitors D-penicillamine and captopril were evaluated. All ulcer models responded pos. to treatments except the ulcers induced by histamine. All kininotropic drugs (except trasylol) had some degree of antiulcer activity, with parmidine being the most effective. The authors suppose that this activity is related to the effects on prostaglandin biosynthesis in the gastric mucosa.
CC 1-9 (Pharmacology)
ST histamine **stomach ulcer** kininotropic drug; ethanol **stomach ulcer** kininotropic drug; reserpine **stomach ulcer** kininotropic drug; diclofenac **stomach ulcer** kininotropic drug; trasylol **stomach ulcer** therapy; cellulose sulfate **stomach ulcer** therapy; parmidine **stomach ulcer** therapy; penicillamine **stomach ulcer** therapy; captopril **stomach ulcer** therapy
IT 50-55-5, Reserpine 51-45-6, Histamine, biological studies 64-17-5, Ethanol, biological studies 15307-79-6, Sodium diclofenac
RL: BIOL (Biological study)
(**stomach ulcer** induced by, kininotropic drug effects on)
IT 52-67-5, D-Penicillamine 1882-26-4, Parmidine 9032-43-3, Cellulose sulfate **62571-86-2**, Captopril
RL: BIOL (Biological study)
(**stomach ulcer** inhibition by)
IT 9087-70-1, Trasylol
RL: BIOL (Biological study)
(**stomach ulcer** response to)

L67 ANSWER 46 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:400488 HCAPLUS
DOCUMENT NUMBER: 97:488
TITLE: Toxicological studies of captopril, an **inhibitor** of **angiotensin converting** enzyme. 2. One month studies on the subacute toxicity of captopril in rats
AUTHOR(S): Imai, Kiyoshi; Yoshimura, Shinsuke; Ohtaki, Tsuneo; Hashimoto, Koroku
CORPORATE SOURCE: Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa, 257, Japan

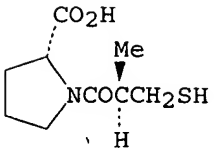
SOURCE: Journal of Toxicological Sciences (**1981**), 6(Suppl. 2), 189-214
CODEN: JTSCDR; ISSN: 0388-1350
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB captopril (I) [**62571-86-2**] orally at 2700 mg/kg/day for 1 mo caused death in 13 of 18 male and 17 of 18 female rats, whereas I at 900 mg/kg/day caused death in 1 of 18 male and 3 of 18 female rats. Dead animals showed marked gastrointestinal tract dilation with multiple hemorrhagic erosions and/or **ulcers** in the glandular **stomach**. Animals receiving 300 mg/kg/day survived but showed polydipsia and polyuria. Animals receiving 10 or 30 mg/kg/day showed no toxicity. Blood urea-N and creatinine were elevated in rats receiving ≥100 mg/kg/day and erythrocyte counts, Hb contents, and hematocrit values were decreased in animals receiving ≥300 mg/kg/day. Afferent arterioles and interlobular arteries in the kidneys were thickened in animals receiving ≥100 mg/kg/day. Extramedullary hematopoiesis and hemosiderosis increased in the spleen and erythropoietic elements increased in the bone marrow of rats receiving ≥100 mg/kg/day. The maximum nontoxic oral dose of I was estimated to be .apprx.30 mg/kg/day in rats.
CC 1-8 (Pharmacology)
IT **62571-86-2**
RL: PRP (Properties)
(toxicity of, sex in relation to)

L67 ANSWER 47 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:400487 HCAPLUS
DOCUMENT NUMBER: 97:487
TITLE: Toxicological studies of captopril, an **inhibitor** of **angiotensin converting** enzyme. 1. Acute toxicological studies of captopril in rats and mice
AUTHOR(S): Imai, Kiyoshi; Hayashi, Yuzo; Hashimoto, Koroku
CORPORATE SOURCE: Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa, 257, Japan
SOURCE: Journal of Toxicological Sciences (**1981**), 6(Suppl. 2), 179-88
CODEN: JTSCDR; ISSN: 0388-1350
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB Oral administration of captopril (I) [**62571-86-2**] caused decreased spontaneous motor activity, lacrimation, salivation, and a decline in body temperature in rats and mice. The LD50 values in male mice, female mice, male rats, and female rats were 4249, 5050, 4336, and 4245 mg/kg, resp. Dead animals had hemorrhagic erosion or **ulcers** in the glandular **stomach**. An i.v. I caused death by dyspnea in some mice within 3 min and delayed death in other animals. The i.p. LD50 values in male and female mice were 3154 and 3225 mg/kg, resp. Mice of both sexes tolerated s.c. I. However, at s.c. injection site necrosis was observed in the skin of rats and mice given 1600 and 1200 I/kg, resp.
CC 1-8 (Pharmacology)
IT **62571-86-2**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of)

L67 ANSWER 48 OF 72 MEDLINE on STN
ACCESSION NUMBER: 2004307576 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15208873
TITLE: [Prophylactic use of angiotensin-converting enzyme inhibitors in indomethacin-induced ulcer and erosion lesions of the stomach].
Profilakticheskoe primenenie ingibitorov angiotenzinprevrashchaiushchego fermenta pri iazvenno-erozivnom porazhenii zheludka, vyzyvaemom indometatsinom.
AUTHOR: Iakubov A V; Usmanova Sh E
SOURCE: Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy, **(2004 Mar)** (2) 47-9.
Journal code: 9601540. ISSN: 1019-5297.
PUB. COUNTRY: Ukraine
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040624
Last Updated on STN: 20041110
Entered Medline: 20041109

AB 75% of patients systematically taking over the period of 6 weeks nonsteroidal anti-inflammatory drugs have their mucous of gastrointestinal tract pathologically changed. This process is called induced NSAID gastropathy. Inhibitors of angiotensin converting enzyme (I-ACE) seems to have gastroprotective effect by enhancing level of endogenous prostaglandins. Besides, an application of I-ACE reduces angiotensin II formation and activates renin-kallicrein-kinin system resulting in nitrogen oxide formation that is in its turn an important component of reparative process of mucous of gastrointestinal tract.
CT Check Tags: Male
Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage
***Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**
Animals

Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use
*Anti-Inflammatory Agents, Non-Steroidal: TO, toxicity
Arthritis, Rheumatoid: DT, drug therapy
Captopril: AD, administration & dosage
Captopril: TU, therapeutic use
Disease Models, Animal
Enalapril: AD, administration & dosage
Enalapril: TU, therapeutic use
English Abstract
Gastric Mucosa: DE, drug effects
Gastric Mucosa: PA, pathology
Indomethacin: TU, therapeutic use
*Indomethacin: TO, toxicity
Lisinopril: AD, administration & dosage
Lisinopril: TU, therapeutic use
Rats
Stomach Ulcer: CI, chemically induced
Stomach Ulcer: PA, pathology
***Stomach Ulcer: PC, prevention & control**
Treatment Outcome
RN 53-86-1 (Indomethacin); **62571-86-2 (Captopril)**; **75847-73-3 (Enalapril)**; **83915-83-7 (Lisinopril)**
CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Anti-Inflammatory Agents, Non-Steroidal)

L67 ANSWER 49 OF 72 MEDLINE on STN
ACCESSION NUMBER: 2004031786 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14732918
TITLE: [Focal segmental glomerulosclerosis with IgA deposits in a patient with **ulcerative colitis**].
Glomerulosclerosi focale segmentale con depositi di IgA in un paziente con rettocolite ulcerosa.
AUTHOR: Fofi C; Nicoletti M C D; Onetti Muda A; Giulio S
CORPORATE SOURCE: U.O. Nefrologia e Dialisi, A.O.S. Camillo-Forlanini, Roma, Italy.. clafofi@tiscali.it
SOURCE: Giornale italiano di nefrologia : organo ufficiale della Societa italiana di nefrologia, **(2003 Nov-Dec)** 20 (6) 641-4.
Journal code: 9426434. ISSN: 0393-5590.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040121
Last Updated on STN: 20040602
Entered Medline: 20040601
AB BACKGROUND: Glomerular diseases are described in patients with active **ulcerative colitis** (UC). Likely drug-induced interstitial nephritis, and nephrotic syndrome due to minimal change disease, have been reported in a few patients with UC on treatment with mesalazine and sulfasalazine (5-ASA).We describe a 33 year-old patient with a 5-years history of UC who recently developed nephrotic syndrome associated with microscopic haematuria. Blood pressure and renal function were normal. The patient was on azathioprine (AZA), mesalazine and sulfasalazine during the last year for his colitis, with good control of bowel disease. Renal biopsy revealed a focal segmental glomerulosclerosis (FSGS) associated with mesangial IgA deposits; no signs of interstitial

nephritis were found. 5-ASA was discontinued, AZA was reduced and a rapid remission of the nephrotic syndrome was observed after 6 weeks of steroid therapy (1 mg/kg/day per os) associated with **ramipril** 5 mg/day, with a follow-up of 9 months. CONCLUSIONS: To our knowledge this is the first report of UC and GSFS associated with IgA deposits. The occurrence of nephrotic syndrome during UC is suggestive of an association between UC and FSGS, but a possible role of mesalazine and /or sulfasalazine in its pathogenesis cannot be excluded. Mesangial IgA deposits could be an "occasional" further occurrence, considering the chronic inflammation of colonic mucosa and the altered immune response of patients with UC.

CT Check Tags: Male
Adult
English Abstract
*Glomerulosclerosis, Focal: CO, complications
Humans
Immunoglobulin A
*Proctocolitis: CO, complications

CN 0 (Immunoglobulin A)

L67 ANSWER 50 OF 72 MEDLINE on STN
ACCESSION NUMBER: 2003372024 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12907340
TITLE: Colonic **ulcers** accompanying collagenous **colitis**: implication of nonsteroidal anti-inflammatory drugs.
AUTHOR: Kakar Sanjay; Pardi Darrell S; Burgart Lawrence J
CORPORATE SOURCE: Department of Pathology, Mayo Clinic, Rochester, Minnesota 55905, USA.
SOURCE: American journal of gastroenterology, **(2003 Aug)** 98 (8) 1834-7.
Journal code: 0421030. ISSN: 0002-9270.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030809
Last Updated on STN: 20030930
Entered Medline: 20030929

AB OBJECTIVES: A small minority of otherwise typical collagenous colitis (CC) patients also have mucosal ulceration (CC-U). We studied the association of CC-U cases with ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs) as a possible explanation for the mucosal ulceration. METHODS: Clinical information and histological features were reviewed in nine cases of biopsy-diagnosed CC-U. Biopsies from 18 unselected cases of CC without ulceration were reviewed for comparison. RESULTS:Of nine patients with CC-U, seven (77.8%) had a history of NSAID ingestion, compared with four of 18 CC controls (20.2%) ($p = 0.006$). The diarrhea resolved after cessation of NSAID use in four CC-U patients, partially resolved in one patient, and persisted in one patient. The outcome was not available in one patient. Of the two CC-U patients who did not use NSAIDs, one patient was taking **lisinopril** (angiotensin-converting enzyme inhibitor), and the diarrhea resolved after stopping the drug; the ulceration in the second patient was thought to be ischemic in origin. CONCLUSIONS: Collagenous **colitis** with **ulceration** has a strong association with NSAID ingestion. Evaluation of medications and cessation of NSAIDs should be considered as a therapeutic option in cases of collagenous **colitis** with colonic **ulceration**.

CT Check Tags: Female; Male

Adult
Aged
Aged, 80 and over
*Anti-Inflammatory Agents, Non-Steroidal: AE, adverse effects
*Colitis: CO, complications
Colitis: DT, drug therapy
Colitis: PA, pathology
Colonoscopy
Humans
*Intestinal Mucosa: PA, pathology
Middle Aged
*Ulcer: CI, chemically induced
*Ulcer: CO, complications
Ulcer: DI, diagnosis
CN 0 (Anti-Inflammatory Agents, Non-Steroidal)

L67 ANSWER 51 OF 72 MEDLINE on STN
ACCESSION NUMBER: 2001420500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11468446
TITLE: **Enalapril**-induced eosinophilic gastroenteritis.
COMMENT: Comment in: J Clin Gastroenterol. 2002 Jul;35(1):105-6.
PubMed ID: 12080243
AUTHOR: Barak N; Hart J; Sitrin M D
CORPORATE SOURCE: University of Chicago, Chicago, Illinois, USA.
SOURCE: Journal of clinical gastroenterology, **(2001 Aug)** 33 (2) 157-8.
Journal code: 7910017. ISSN: 0192-0790.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB Eosinophilic gastroenteritis is a rare disorder of unknown etiology. We describe a case of a 63-year-old woman with **chronic diarrhea** and eosinophilia. Small bowel biopsy revealed eosinophils in large clusters in the lamina propria with focal infiltration of the epithelium. The patient's diarrhea and eosinophilia started shortly after **enalapril** was prescribed. When the patient was instructed to stop taking that drug, her diarrhea promptly ceased, and the blood eosinophil level returned to normal. This is the first reported case of eosinophilic gastroenteritis associated with an angiotensin-converting enzyme inhibitor. Eosinophilic gastroenteritis should be entertained in the differential diagnosis of patients taking angiotensin-converting enzyme inhibitors who develop diarrhea or other gastrointestinal symptoms.

CT Check Tags: Female
Biopsy
Diagnosis, Differential
Diarrhea: ET, etiology
Enalapril: AD, administration & dosage
***Enalapril: AE, adverse effects**
*Eosinophilia: CI, chemically induced
Eosinophilia: DI, diagnosis
Eosinophilia: PA, pathology
*Gastroenteritis: CI, chemically induced

Gastroenteritis: DI, diagnosis
Gastroenteritis: PA, pathology
Humans
*Hypertension: DT, drug therapy
Intestinal Mucosa: DE, drug effects
Intestinal Mucosa: PA, pathology
Middle Aged
RN **75847-73-3 (Enalapril)**

L67 ANSWER 52 OF 72 MEDLINE on STN
ACCESSION NUMBER: 2000205446 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10741273
TITLE: The relationship between angiogenesis and the immune response in carcinogenesis and the progression of malignant disease.
AUTHOR: O'Byrne K J; Dalgleish A G; Browning M J; Steward W P; Harris A L
CORPORATE SOURCE: University Department of Oncology, Leicester Royal Infirmary, UK.. kobyrne@lri.org.uk
SOURCE: European journal of cancer (Oxford, England : 1990), **(2000 Jan)** 36 (2) 151-69. Ref: 263
Journal code: 9005373. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000407

AB Recent studies have demonstrated that angiogenesis and suppressed cell-mediated immunity (CMI) play a central role in the pathogenesis of malignant disease facilitating tumour growth, invasion and metastasis. In the majority of tumours, the malignant process is preceded by a pathological condition or exposure to an irritant which itself is associated with the induction of angiogenesis and/or suppressed CMI. These include: cigarette smoking, chronic bronchitis and lung cancer; chronic oesophagitis and oesophageal cancer; chronic viral infections such as human papilloma virus and ano-genital cancers, chronic hepatitis B and C and hepatocellular carcinoma, and Epstein-Barr virus (EBV) and lymphomas; chronic inflammatory conditions such as Crohn's disease and **ulcerative colitis** and colorectal cancer; asbestos exposure and mesothelioma and excessive sunlight exposure/sunburn and malignant melanoma. Chronic exposure to growth factors (insulin-like growth factor-I in acromegaly), mutations in tumour suppressor genes (TP53 in Li Fraumeni syndrome) and long-term exposure to immunosuppressive agents (cyclosporin A) may also give rise to similar environments and are associated with the development of a range of solid tumours. The increased blood supply would facilitate the development and proliferation of an abnormal clone or clones of cells arising as the result of: (a) an inherited genetic abnormality; and/or (b) acquired somatic mutations, the latter due to local production and/or enhanced delivery of carcinogens and mutagenic growth factors. With progressive detrimental mutations and growth-induced tumour hypoxia, the transformed cell, to a lesser or greater extent, may amplify the angiogenic process and CMI suppression, thereby facilitating further tumour growth and metastasis. There is accumulating evidence that long-term treatment with cyclo-oxygenase

inhibitors (aspirin and indomethacin), cytokines such as interferon-alpha, anti-oestrogens (tamoxifen and raloxifene) and **captopril** significantly reduces the incidence of solid tumours such as breast and colorectal cancer. These agents are anti-angiogenic and, in the case of aspirin, indomethacin and interferon-alpha have proven immunomodulatory effects. Collectively these observations indicate that angiogenesis and suppressed CMI play a central role in the development and progression of malignant disease.

CT Disease Progression
Gene Silencing
Genes, p53: IM, immunology
Humans
Hygiene
*Neoplasms: BS, blood supply
Neoplasms: DT, drug therapy
Neoplasms: IM, immunology
*Neovascularization, Pathologic: ET, etiology
Neovascularization, Pathologic: IM, immunology
Prostaglandin-Endoperoxide Synthase: IM, immunology
Receptors, Interferon: IM, immunology
Research Support, Non-U.S. Gov't

CN 0 (Receptors, Interferon); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L67 ANSWER 53 OF 72 MEDLINE on STN
ACCESSION NUMBER: 1998445718 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9772541
TITLE: The decrease of gastric mucosal blood flow in obstructive jaundice under stress.
AUTHOR: Yang N; Xu W; Duan J
CORPORATE SOURCE: Department of Surgery, People's Hospital, Beijing Medical University.
SOURCE: Zhonghua yi xue za zhi, **(1997 Sep)** 77 (9) 692-4.
Journal code: 7511141. ISSN: 0376-2491.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981109

AB OBJECTIVE: To investigate the cause of decrease of gastric mucosal blood flow (GMBF) in obstructive jaundice under stress. METHODS: With common bile duct ligation (CBDL) in Wistar rats under cold restraint stress, GMBF and the content of Endothelin-1, Angiotensin-II, H2, alpha 1 receptor in gastric mucosa were measured. Before stress anti-ET-1 serum, **Enalapril**, Cimentidine and Phetolamins were administrated, and the change of GMBF was studied. RESULTS: GMBF was significantly decreased in CBDL in stress than those in control subjects. The content of ET1 and Ang-II was significantly increaced, the density of H2 and alpha 1 receptor was significantly decreased. Before stress antagonist was administrated, and GMBF was significantly increased. CONCLUSION: GMBF was decreased by increased ET, Ang-II and decreased H2, alpha 1 receptor in CBDL, under stress. Antagonist improved gastric mucosal blood flow. They had protection from gastric mucosa.

CT Check Tags: Male
Angiotensin II: ME, metabolism
Animals

*Cholestasis: PP, physiopathology
Cold
*Endothelin-1: ME, metabolism
English Abstract
*Gastric Mucosa: BS, blood supply
Rats
Rats, Wistar
Receptors, Histamine H2: ME, metabolism
Regional Blood Flow
Stomach Ulcer: PC, prevention & control
Stress
RN 11128-99-7 (Angiotensin II)
CN 0 (Endothelin-1); 0 (Receptors, Histamine H2)

L67 ANSWER 54 OF 72 MEDLINE on STN
ACCESSION NUMBER: 1998220075 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9559321
TITLE: The effects of **captopril** and naloxone on restraint-cold-stress- and ethanol-induced gastric lesions in rats.
AUTHOR: Uluoglu C; Guney Z; Kilinc M; Bozkurt S; Ercan Z S
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Gazi University, Ankara, Turkey.
SOURCE: General pharmacology, **(1998 May)** 30 (5) 701-4.
Journal code: 7602417. ISSN: 0306-3623.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980519

AB 1. This study was undertaken to investigate the effect of **captopril** (1 microgram/kg or 1 mg/kg, i.p.) on the actions of naloxone (5 mg/kg, i.p. in gastric ulceration induced by ethanol and restraint-cold-stress. 2. Neither naloxone (5 mg/kg, i.p.) nor **captopril** (1 mg/kg, i.p.) alone induced any change in the indices of the ulcer in either group. 3. **Captopril** at a lower dose (1 microgram/kg, i.p.), when combined with naloxone (5 mg/kg, i.p.), significantly reduced cumulative ulcer length only in the ethanol-treated group (from 54.9 +/- 7.2 mm to 22.5 +/- 6.2 mm). 4. However, a high dose of **captopril** (1 mg/kg) plus naloxone pretreatment caused a significant reduction in both ethanol (from 54.9 +/- 7.2 mm to 24.9 +/- 6.5 mm) and restraint-cold-stress (from 19.0 +/- 3.0 mm to 5.3 +/- 1.0 mm)-induced ulcer formation. 5. Acetylsalycilic acid, when used together with **captopril**, increased the ulcer formation induced by stress. 6. Naloxone, by increasing the release of prostaglandins, has been shown to prevent ulcer formation induced by several noxious stimuli. 7. Therefore, the effect of the combination might be due to the synergistic interaction of both drugs on prostaglandin synthesis.

CT Check Tags: Female; Male
Angiotensin-Converting Enzyme Inhibitors: PD, pharmacology
***Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**
Animals
Captopril: PD, pharmacology
***Captopril: TU, therapeutic use**
Drug Synergism
Drug Therapy, Combination

Ethanol
Naloxone: PD, pharmacology
*Naloxone: TU, therapeutic use
Prostaglandins: ME, metabolism
Rats
Restraint, Physical
***Stomach Ulcer: DT, drug therapy**
Stomach Ulcer: ET, etiology
Stress
RN 465-65-6 (Naloxone); **62571-86-2 (Captopril)**; 64-17-5 (Ethanol)
CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Prostaglandins)

L67 ANSWER 55 OF 72 MEDLINE on STN
ACCESSION NUMBER: 97162131 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9009118
TITLE: Cigarette smoke increases gastric ulcer size in part by an angiotensin II-mediated mechanism in rats.
AUTHOR: Seno K; Zhu J H; Barrett J D; Eggena P; Scremin O U; Lam K; Leung J W; Leung F W
CORPORATE SOURCE: Gastroenterology Laboratory, Sepulveda and West Los Angeles Veterans Administration Medical Center California, 91343, USA.
SOURCE: Digestive diseases and sciences, **(1997 Jan)** 42 (1) 74-8.
Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970219

AB To assess the mechanism of the effect of cigarette smoke on ulcer disease we employed a rat model in which cigarette smoke increases the size of acetic acid-induced gastric ulcer and decreases the hyperemia at the ulcer margin. We postulate that cigarette smoke increases angiotensin II (a vasoconstrictor) in ulcer tissue. Since direct measurement of angiotensin II in small tissue samples is problematic, we compared the messenger ribonucleic acid (mRNA) for its precursors (angiotensinogen and renin) in ulcer and normal gastric tissue. We also evaluated the effect of **enalapril**, which blocks the conversion of angiotensin I to angiotensin II on ulcer size. In the ulcer tissue, cigarette smoke produced a significant increase in mRNA for angiotensinogen but not for renin. **Enalapril** decreased the size of the gastric ulcer in rats exposed to cigarette smoke. The data support the possibility that in ulcer tissue cigarette smoke stimulates an angiotensin II-mediated mechanism, which may in part be responsible for the impairment of ulcer margin hyperemia and aggravation of ulcer size.

CT Check Tags: Male
Angiotensin II: ME, metabolism
*Angiotensin II: PH, physiology
Angiotensin-Converting Enzyme Inhibitors: PD, pharmacology
Animals
Enalapril: PD, pharmacology
Immunoblotting
Platelet-Derived Growth Factor: AN, analysis
RNA, Messenger: AN, analysis
Rats

Rats, Sprague-Dawley
Renin: AN, analysis
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, Non-P.H.S.
*Smoking: AE, adverse effects
Somatomedins: AN, analysis
Stomach Ulcer: CI, chemically induced
Stomach Ulcer: ME, metabolism
***Stomach Ulcer: PA, pathology**
Transforming Growth Factor beta: AN, analysis
RN 11128-99-7 (Angiotensin II); **75847-73-3 (Enalapril)**
CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Platelet-Derived Growth Factor); 0 (RNA, Messenger); 0 (Somatomedins); 0 (Transforming Growth Factor beta); EC 3.4.23.15 (Renin)

L67 ANSWER 56 OF 72 MEDLINE on STN
ACCESSION NUMBER: 96105748 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8550131
TITLE: Effect of angiotensin converting enzyme inhibitor (**captopril**) on gastric ulcer production in pylorus ligated rats.
AUTHOR: Rao S P; Sathiamoorthy A; Sathiamoorthy S S
CORPORATE SOURCE: Department of Physiology, Kasturba Medical College, Manipal.
SOURCE: Indian journal of physiology and pharmacology, **(1995 Jul)** 39 (3) 296-8.
Journal code: 0374707. ISSN: 0019-5499.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960306
Last Updated on STN: 19960306
Entered Medline: 19960220
AB Intraperitoneal injection of Angiotensin Converting Enzyme inhibitor, **captopril**, reduced significantly ($P < 0.001$), the production of gastric ulcers in pylorus-ligated albino rats, compared to the control groups, irrespective of the dose schedule--single or quadruple. In the light of evidence available in the literature, it is reasonable to hypothesise that the anti-ulcer effect of **captopril** may be mediated through prostaglandins.
CT Check Tags: Female; Male
Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage
***Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**
Animals
Anti-Ulcer Agents: AD, administration & dosage
*Anti-Ulcer Agents: TU, therapeutic use
Captopril: AD, administration & dosage
***Captopril: TU, therapeutic use**
Injections, Intraperitoneal
Pylorus: PH, physiology
Rats
Rats, Wistar
Stomach Ulcer: PA, pathology
***Stomach Ulcer: PC, prevention & control**
RN **62571-86-2 (Captopril)**
CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Anti-Ulcer Agents)

L67 ANSWER 57 OF 72 MEDLINE on STN
ACCESSION NUMBER: 94300666 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8028057
TITLE: **Captopril** decreases stress ulceration without affecting gastric perfusion during canine hemorrhagic shock.
AUTHOR: Cullen J J; Ephgrave K S; Broadhurst K A; Booth B
CORPORATE SOURCE: Department of Surgery, VA Medical Center, Iowa City, IA 52246.
SOURCE: Journal of trauma, **(1994 Jul)** 37 (1) 43-9.
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19940818
Entered Medline: 19940811

AB The renin-angiotensin axis has recently been called the source of disproportionate splanchnic vasoconstriction during shock, and blocking this axis decreased gastric stress ulceration during swine cardiogenic shock. The present study tested whether the angiotensin converting enzyme inhibitor **captopril** would prevent stress ulceration when given after the onset of canine hemorrhagic shock, and whether any detrimental effects would result from enhancing splanchnic perfusion with **captopril** during hemorrhagic shock. We found that **captopril** treatment was associated with a decrease in gastric mucosal injury and with a marked decrease in systemic acidosis. **Captopril** enhanced blood flow to the small intestine, pancreas, liver, and spleen, but not flow to the stomach, during shock. Following the reinfusion of shed blood, the **captopril**-treated animals had decreased mean blood pressures and increased heart rates compared with untreated animals. We found **captopril** alleviated the stress ulceration produced by canine hemorrhagic shock, but concluded that the likely mechanism was alleviating systemic acidosis through enhanced perfusion of other viscera rather than a specific enhancement of gastric perfusion.

CT Analysis of Variance
Animals
***Captopril: TU, therapeutic use**
Disease Models, Animal
Dogs
Gastric Mucosa: DE, drug effects
Regional Blood Flow: DE, drug effects
Regression Analysis
Research Support, U.S. Gov't, Non-P.H.S.
*Shock, Hemorrhagic: CO, complications
Shock, Hemorrhagic: PP, physiopathology
Splanchnic Circulation: DE, drug effects
Stomach Ulcer: ET, etiology
Stomach Ulcer: PP, physiopathology
***Stomach Ulcer: PC, prevention & control**
*Stress: CO, complications
Stress: PP, physiopathology
Treatment Outcome

RN **62571-86-2 (Captopril)**

L67 ANSWER 58 OF 72 MEDLINE on STN
ACCESSION NUMBER: 91139209 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2286425
TITLE: Comparison of the effects of **captopril** and **enalapril** on oxyphenbutazone and ethanol-induced gastric lesions in rats.
AUTHOR: D'Souza R S; Bhounsule S A; Dhume V G
CORPORATE SOURCE: Department of Pharmacology, Goa Medical College, Bambolin.
SOURCE: Indian journal of physiology and pharmacology, **(1990 Jul)** 34 (3) 206-8.
Journal code: 0374707. ISSN: 0019-5499.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19980206
Entered Medline: 19910325

AB We have compared the effect of the converting enzyme inhibitors, **captopril** and **enalapril**, on two models of gastric ulcers, viz; ethanol and oxyphenbutazone-induced lesions in rats. Both **captopril** and **enalapril** did not affect ethanol-induced lesions. While **captopril** significantly protected against oxyphenbutazone-induced lesions, **enalapril** aggravated the lesions. This difference is probably due to the lack of the protective sulfhydryl group in the chemical structure of **enalapril**.

CT Check Tags: Comparative Study; Male
Animals
***Captopril: PD, pharmacology**
***Enalapril: PD, pharmacology**
*Ethanol
*Oxyphenbutazone
Rats
Rats, Inbred Strains
Stomach Ulcer: CI, chemically induced
***Stomach Ulcer: PC, prevention & control**

RN 129-20-4 (Oxyphenbutazone); **62571-86-2 (Captopril)**; 64-17-5 (Ethanol); **75847-73-3 (Enalapril)**

L67 ANSWER 59 OF 72 MEDLINE on STN
ACCESSION NUMBER: 90255525 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2187703
TITLE: Effect of **captopril** on oxyphenbutazone and ethanol-induced gastric lesions in rats.
AUTHOR: Bhounsule S A; Pereira J S; Hede S S; Diniz D'Souza R S
CORPORATE SOURCE: Department of Pharmacology, Goa Medical College, Bambolim, India.
SOURCE: European journal of pharmacology, **(1990 Feb 20)** 177 (1-2) 87-90.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900720
Last Updated on STN: 19980206
Entered Medline: 19900628

AB We studied the effect of the angiotensin converting enzyme inhibitor, **captopril**, on two models of gastric ulcers; oxyphenbutazone and ethanol-induced lesions. There was a significant protective effect against oxyphenbutazone-induced ulcers, which was prevented by prior administration of indomethacin. **Captopril**, however, failed to protect against ethanol-induced lesions. These findings are discussed in the light of **captopril** being a sulfhydryl compound with prostaglandin-releasing activity.

CT Check Tags: Male
Animals
***Captopril: PD, pharmacology**
*Ethanol
Indomethacin: PD, pharmacology
*Oxyphenbutazone
Rats
Rats, Inbred Strains
Stomach Ulcer: CI, chemically induced
***Stomach Ulcer: PC, prevention & control**

RN 129-20-4 (Oxyphenbutazone); 53-86-1 (Indomethacin); **62571-86-2 (Captopril)**; 64-17-5 (Ethanol)

L67 ANSWER 60 OF 72 MEDLINE on STN
ACCESSION NUMBER: 80208887 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6104247
TITLE: Neurological dysfunction in two patients receiving **captopril** and cimetidine.
AUTHOR: Atkinson A B; Brown J J; Lever A F; McAreavey D; Robertson J I; Behan P O; Melville I D; Weir A I
SOURCE: Lancet, **(1980 Jul 5)** 2 (8184) 36-7.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198008
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 20000303
Entered Medline: 19800828

CT Check Tags: Female; Male
***Captopril: AE, adverse effects**
*Cimetidine: AE, adverse effects
*Guanidines: AE, adverse effects
Humans
Hypertension: DT, drug therapy
Middle Aged
*Peripheral Nervous System Diseases: CI, chemically induced
*Polyradiculoneuropathy: CI, chemically induced
*Proline: AA, analogs & derivatives
Stomach Ulcer: DT, drug therapy

RN 147-85-3 (Proline); 51481-61-9 (Cimetidine); **62571-86-2 (Captopril)**
CN 0 (Guanidines)

L67 ANSWER 61 OF 72 MEDLINE on STN
ACCESSION NUMBER: 79071878 MEDLINE
DOCUMENT NUMBER: PubMed ID: 82838
TITLE: Serum angiotensin-converting enzyme (SACE) in sarcoidosis and other granulomatous disorders.

AUTHOR: Studdy P; Bird R; James D G
SOURCE: Lancet, **(1978 Dec 23-30)** 2 (8104-5) 1331-4.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197902
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19980206
Entered Medline: 19790223

AB Serum angiotensin-converting enzyme (SACE) activity was significantly higher in 90 patients with sarcoidosis (55 +/- [S.D.] 23 nmol min-1 ml-1) than in 80 healthy controls (34 +/- 9 nmol min-1 ml-1). Steroid therapy modified SACE activity; 60 sarcoidosis patients who were not being treated with steroids had significantly higher enzyme activities (58 +/- 24 nmol min-1 ml-1) than 30 steroid-treated sarcoidosis patients (40 +/- 19 nmol min-1 ml-1). In 50% of the non-steroid treated sarcoidosis patients SACE activity was more than 2 S.D. above the mean value for the controls. SACE activity was measured in 22 tuberculous patients (38 +/- 14 nmol min-1 ml-1), 20 leprosy patients (34 +/- 9 nmol min-1 ml-1), 31 with primary biliary cirrhosis (44 +/- 20 nmol min-1 ml-1), 26 with **inflammatory bowel** disease (31 +/- 9 nmol min-1 ml-1), 8 with hepatic granulomatous disease, 5 with Hodgkin's disease, and 2 with schistosomiasis. The combined false-positive rate for these non-sarcoidosis patients was 10%. Serial SACE assays provide useful information on the course of sarcoidosis and response to steroid treatment.

CT Check Tags: Female; Male
Acute Disease
Adolescent
Adult
Aged
Angiotensin-Converting Enzyme Inhibitors
Chronic Disease
Enteritis: EN, enzymology
Enzyme Inhibitors
Granuloma: EN, enzymology
Hodgkin Disease: EN, enzymology
Humans
Leprosy: EN, enzymology
Liver Cirrhosis, Biliary: EN, enzymology
Liver Diseases: EN, enzymology
Middle Aged
*Peptidyl-Dipeptidase A: BL, blood
Prednisolone: TU, therapeutic use
Sarcoidosis: DT, drug therapy
*Sarcoidosis: EN, enzymology
Schistosomiasis: EN, enzymology
Tuberculosis, Pulmonary: EN, enzymology

RN 50-24-8 (Prednisolone)
CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Enzyme Inhibitors); EC 3.4.15.1 (Peptidyl-Dipeptidase A)

L67 ANSWER 62 OF 72 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004506805 EMBASE
TITLE: Models for evaluating agents intended for the prophylaxis, mitigation and treatment of radiation injuries report of an

NCI workshop, December 3-4, 2003.

AUTHOR: Stone H.B.; Moulder J.E.; Coleman C.N.; Ang K.K.; Anscher M.S.; Barcellos-Hoff M.H.; Dynan W.S.; Fike J.R.; Grdina D.J.; Greenberger J.S.; Hauer-Jensen M.; Hill R.P.; Kolesnick R.N.; MacVittie T.J.; Marks C.; McBride W.H.; Metting N.; Pellmar T.; Purucker M.; Robbins M.E.; Schiestl R.H.; Seed T.M.; Tomaszewski J.E.; Travis E.L.; Wallner P.E.; Wolpert M.; Zaharevitz D.

CORPORATE SOURCE: H.B. Stone, EPN 6015A, MSC 7440, 6130 Executive Blvd., Bethesda, MD 20892-7440, United States. stoneh@mail.nih.gov

SOURCE: Radiation Research, (2004) Vol. 162, No. 6, pp. 711-728.
Refs: 199
ISSN: 0033-7587 CODEN: RAREAE

COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041230
Last Updated on STN: 20041230

AB To develop approaches to prophylaxis/protection, mitigation and treatment of radiation injuries, appropriate models are needed that integrate the complex events that occur in the radiation-exposed organism. While the spectrum of agents in clinical use or preclinical development is limited, new research findings promise improvements in survival after whole-body irradiation and reductions in the risk of adverse effects of radiotherapy. Approaches include agents that act on the initial radiochemical events, agents that prevent or reduce progression of radiation damage, and agents that facilitate recovery from radiation injuries. While the mechanisms of action for most of the agents with known efficacy are yet to be fully determined, many seem to be operating at the tissue, organ or whole animal level as well as the cellular level. Thus research on prophylaxis/protection, mitigation and treatment of radiation injuries will require studies in whole animal models. Discovery, development and delivery of effective radiation modulators will also require collaboration among researchers in diverse fields such as radiation biology, inflammation, physiology, toxicology, immunology, tissue injury, drug development and radiation oncology. Additional investment in training more scientists in radiation biology and in the research portfolio addressing radiological and nuclear terrorism would benefit the general population in case of a radiological terrorism event or a large-scale accidental event as well as benefit patients treated with radiation.

CT Medical Descriptors:
*radiation injury: CO, complication
*radiation injury: DT, drug therapy
*radiation injury: PC, prevention
radiation protection
cancer radiotherapy
radiation dose fractionation
radiation response
hematologic disease: CO, complication
hematologic disease: DT, drug therapy
digestive system injury: CO, complication
digestive system injury: DT, drug therapy

central nervous system disease: CO, complication
central nervous system disease: DT, drug therapy
lung injury: CO, complication
lung injury: DT, drug therapy
lung injury: PC, prevention
kidney injury: CO, complication
kidney injury: DT, drug therapy
kidney injury: PC, prevention
xerostomia: CO, complication
xerostomia: DT, drug therapy
xerostomia: PC, prevention
proctitis: CO, complication
proctitis: DT, drug therapy
gastrointestinal hemorrhage: SI, side effect
lung fibrosis: DT, drug therapy
lung fibrosis: PC, prevention
kidney disease: CO, complication
kidney disease: DT, drug therapy
fibrosis: CO, complication
fibrosis: DT, drug therapy
whole body radiation
radiation hazard
human
nonhuman
clinical trial
conference paper
priority journal
Drug Descriptors:
*radioprotective agent: AE, adverse drug reaction
*radioprotective agent: CT, clinical trial
*radioprotective agent: AD, drug administration
*radioprotective agent: DO, drug dose
*radioprotective agent: DT, drug therapy
*radioprotective agent: IV, intravenous drug administration
*radioprotective agent: PD, pharmacology
dipeptidyl carboxypeptidase inhibitor: CT, clinical trial
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
amifostine: CT, clinical trial
amifostine: AD, drug administration
amifostine: DO, drug dose
amifostine: DT, drug therapy
amifostine: IV, intravenous drug administration
amifostine: PD, pharmacology
pentoxifylline: DT, drug therapy
hemopoietic growth factor: DT, drug therapy
Fas antigen: EC, endogenous compound
androstenediol: DT, drug therapy
interleukin 11: DT, drug therapy
keratinocyte growth factor: DT, drug therapy
angiotensin: DT, drug therapy
antibiotic agent: DT, drug therapy
salazosulfapyridine: DT, drug therapy
octreotide: DT, drug therapy
misoprostol: DT, drug therapy
enema: DT, drug therapy
sucralfate: DT, drug therapy
short chain fatty acid: DT, drug therapy
antioxidant: DT, drug therapy

antioxidant: PD, pharmacology
fibroblast growth factor: DT, drug therapy
fibroblast growth factor: PD, pharmacology
thrombomodulin: EC, endogenous compound
anticoagulant agent: AE, adverse drug reaction
anticoagulant agent: DT, drug therapy
manganese superoxide dismutase: DT, drug therapy
protein p53: EC, endogenous compound
angiotensin 2 receptor antagonist: DT, drug therapy
dexamethasone: DT, drug therapy
mercaptamine: DT, drug therapy
transforming growth factor beta: EC, endogenous compound
halofuginone: DT, drug therapy
halofuginone: PD, pharmacology
primrose oil: DT, drug therapy
primrose oil: PD, pharmacology
primrose oil: TP, topical drug administration
unindexed drug

RN (amifostine) 20537-88-6; (pentoxifylline) 6493-05-6; (androstenediol) 28652-91-7, 521-17-5; (keratinocyte growth factor) 126469-10-1; (**angiotensin**) 11128-99-7, 1407-47-2; (salazosulfapyridine) 599-79-1; (octreotide) 83150-76-9; (misoprostol) 59122-46-2, 59122-48-4; (sucralfate) 54182-58-0; (fibroblast growth factor) 62031-54-3; (thrombomodulin) 112049-68-0; (dexamethasone) 50-02-2; (mercaptamine) 156-57-0, 60-23-1; (halofuginone) 55837-20-2, 64924-67-0, 7695-84-3; (primrose oil) 65546-85-2

CN Wr 2721

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ACCESSION NUMBER: 2004465928 EMBASE
TITLE: Diabetes mellitus and pregnancy: The GP's role.
AUTHOR: Cheung W.; McElduff A.
CORPORATE SOURCE: Dr. W. Cheung, Department of Diabetes/Endocrinology, Westmead Hospital, Sydney, NSW, Australia
SOURCE: Medicine Today, (2004) Vol. 5, No. 10, pp. 16-22. ISSN: 1443-430X CODEN: MTNBCV
COUNTRY: Australia
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041119
Last Updated on STN: 20041119

AB • Pregnancy outcomes in patients With diabetes can be optimised by appropriate care. Preconception counselling and meticulous glycaemic control before and during pregnancy are essential. • Patients need assessment for the presence of micro- and macrovascular complications of diabetes. Some of these need therapy before pregnancy (e.g. retinopathy) while others increase the likelihood of problems in pregnancy (e.g. autonomic neuropathy or nephropathy) or place the mother's health at increased risk (e.g. macrovascular disease). • Postpartum counselling and adjustment of insulin therapy is required to ensure patient safety. • Drug therapy, including complementary therapy, should be reviewed.

CT Medical Descriptors:
*maternal diabetes mellitus: DT, drug therapy

gestation period
maternal care
general practitioner
patient counseling
congenital disorder: CO, complication
congenital disorder: CN, congenital disorder
perinatal mortality
hemoglobin determination
risk assessment
statistical analysis
statistical significance
macrosomia: CO, complication
macrosomia: CN, congenital disorder
hypoglycemia: CO, complication
hypoglycemia: CN, congenital disorder
preeclampsia: CO, complication
preeclampsia: CN, congenital disorder
drug safety
drug contraindication
patient education
hypertension: DT, drug therapy
glucose blood level
thyroid function test
hypothyroidism: CO, complication
celiac disease: CO, complication
practice guideline
puerperium
breast feeding
human
female
fetus
newborn
adult
review
Drug Descriptors:
hemoglobin A1c: EC, endogenous compound
oral antidiabetic agent: DT, drug therapy
oral antidiabetic agent: PO, oral drug administration
insulin: DT, drug therapy
metformin: DT, drug therapy
metformin: PO, oral drug administration
dipeptidyl carboxypeptidase inhibitor
angiotensin receptor antagonist
diuretic agent
beta adrenergic receptor blocking agent
methyldopa: DT, drug therapy
hydralazine: DT, drug therapy
verapamil: DT, drug therapy
antilipemic agent
isophane insulin: DT, drug therapy
insulin zinc suspension: DT, drug therapy
insulin[B28 lysine B29 proline]: DT, drug therapy
insulin aspart: DT, drug therapy
insulin glargine: DT, drug therapy
thyrotropin: EC, endogenous compound
neutral insulin: DT, drug therapy
hypurin neutral
hypurin isophane
humulin l

humulin ul
RN (hemoglobin A1c) 62572-11-6; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (methyldopa) 555-29-3, 555-30-6; (hydralazine) 304-20-1, 86-54-4; (verapamil) 152-11-4, 52-53-9; (isophane insulin) 9004-17-5; (insulin zinc suspension) 8049-62-5; (insulin[B28 lysine B29 proline]) 133107-64-9; (insulin aspart) 116094-23-6; (insulin glargine) 160337-95-1; (thyrotropin) 9002-71-5; (neutral insulin) 9004-14-2
CN Actrapid; Humulin r; Hypurin neutral; Hypurin isophane; Protaphane; Monotard; Humulin l; Ultratard; Humulin ul; Humalog; Novorapid; Lantus

L67 ANSWER 64 OF 72 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003483636 EMBASE
TITLE: Scleroderma: A treatable disease.
AUTHOR: Korn J.H.
CORPORATE SOURCE: Dr. J.H. Korn, Rheumatology Section, Boston University Medical Center, 80 East Concord Street, Boston, MA 02118, United States
SOURCE: Cleveland Clinic Journal of Medicine, (2003) Vol. 70, No. 11, pp. 954-968.
Refs: 9
ISSN: 0891-1150 CODEN: CCJMEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
028 Urology and Nephrology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20031211
Last Updated on STN: 20031211
AB Many effective treatments for scleroderma have emerged in recent years, including bosentan, an endothelin receptor antagonist, and epoprostenol, a prostacyclin, both of which target vasoconstriction. Cyclophosphamide may soon be proven effective against interstitial lung disease.
CT Medical Descriptors:
*scleroderma: DI, diagnosis
*scleroderma: DT, drug therapy
*scleroderma: PC, prevention
*scleroderma: TH, therapy
treatment planning
interstitial lung disease: CO, complication
interstitial lung disease: DI, diagnosis
interstitial lung disease: DT, drug therapy
vasoconstriction
survival rate
clinical feature
kidney disease: CO, complication
kidney disease: DI, diagnosis
kidney disease: DT, drug therapy
lung disease: CO, complication
Raynaud phenomenon: DT, drug therapy
Raynaud phenomenon: TH, therapy
vascular disease
blood vessel injury
warming

skin ulcer: DT, drug therapy
superinfection: DT, drug therapy
blood pressure monitoring
urinalysis
hypertension: DI, diagnosis
hypertension: DT, drug therapy
proteinuria: DI, diagnosis
proteinuria: DT, drug therapy
bronchiectasis: CO, complication
aspiration pneumonia: CO, complication
pleura disease: CO, complication
pleura effusion: CO, complication
fibrosing alveolitis: CO, complication
fibrosing alveolitis: DI, diagnosis
fibrosing alveolitis: DT, drug therapy
computer assisted tomography
lung function test
lung biopsy
pulmonary hypertension: CO, complication
pulmonary hypertension: DT, drug therapy
syndrome CREST
quality of life
skin manifestation: SI, side effect
gastrointestinal disease: DT, drug therapy
gastrointestinal reflux: DT, drug therapy
chronic diarrhea: DT, drug therapy
stomach antrum vascular ectasia: SU, surgery
laser surgery
cardiovascular disease
fibrosis
human
clinical trial
article
Drug Descriptors:
bosentan: DT, drug therapy
bosentan: PD, pharmacology
endothelin receptor antagonist: DT, drug therapy
endothelin receptor antagonist: PD, pharmacology
prostacyclin: CT, clinical trial
prostacyclin: DT, drug therapy
prostacyclin: PD, pharmacology
prostacyclin derivative: AE, adverse drug reaction
prostacyclin derivative: CT, clinical trial
prostacyclin derivative: DT, drug therapy
prostacyclin derivative: IH, inhalational drug administration
prostacyclin derivative: IV, intravenous drug administration
prostacyclin derivative: SC, subcutaneous drug administration
cyclophosphamide: DT, drug therapy
cyclophosphamide: PD, pharmacology
carbon monoxide
calcium channel blocking agent: DT, drug therapy
alpha adrenergic receptor blocking agent: DT, drug therapy
glyceryl trinitrate: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
antibiotic agent: DT, drug therapy
cefalexin: DT, drug therapy
dicloxacillin: DT, drug therapy
ciprofloxacin: DT, drug therapy

vasodilator agent: DT, drug therapy
vasodilator agent: IH, inhalational drug administration
vasodilator agent: IA, intraarterial drug administration
sildenafil: DT, drug therapy
angiotensin receptor antagonist: DT, drug therapy
creatinine: EC, endogenous compound
bone morphogenetic protein 2: EC, endogenous compound
angiopoietin 1: EC, endogenous compound
angiopoietin 2: EC, endogenous compound
anticoagulant agent: DT, drug therapy
uniprost: AE, adverse drug reaction
uniprost: DT, drug therapy
uniprost: SC, subcutaneous drug administration
nitric oxide: DT, drug therapy
nitric oxide: IH, inhalational drug administration
iloprost: DT, drug therapy
iloprost: IH, inhalational drug administration
endothelin: EC, endogenous compound
placebo
proton pump inhibitor: DT, drug therapy
histamine H2 receptor antagonist: DT, drug therapy
unindexed drug

RN (bosentan) 147536-97-8, 157212-55-0; (prostacyclin) 35121-78-9, 61849-14-7; (cyclophosphamide) 50-18-0; (carbon monoxide) 630-08-0; (glyceryl trinitrate) 55-63-0; (cefalexin) 15686-71-2, 23325-78-2; (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (ciprofloxacin) 85721-33-1; (sildenafil) 139755-83-2; (creatinine) 19230-81-0, 60-27-5; (angiopoietin 1) 186270-49-5; (angiopoietin 2) 194368-66-6; (uniprost) 81846-19-7; (nitric oxide) 10102-43-9; (iloprost) 78919-13-8, 82889-99-4

CN Flolan; Viagra; Tracleer; Cytoxan; Neosar; Remodulin; Ilomedin

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ACCESSION NUMBER: 2003277210 EMBASE
TITLE: Steroid therapy reduces mesangial matrix accumulation in advanced IgA nephropathy.
AUTHOR: Kuriki M.; Asahi K.; Asano K.; Sakurai K.; Eiro M.; Suzuki H.; Watanabe K.; Katoh T.; Watanabe T.
CORPORATE SOURCE: Dr. T. Katoh, Department of Internal Medicine III, Fukushima Medical Univ. Sch. of Med., 1 Hikarigaoka, Fukushima 960-1295, Japan. t-katoh@fmu.ac.jp
SOURCE: Nephrology Dialysis Transplantation, (1 Jul 2003) Vol. 18, No. 7, pp. 1311-1315.
Refs: 16
ISSN: 0931-0509 CODEN: NDTREA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030731
Last Updated on STN: 20030731

AB Background. Steroid therapy for IgA nephropathy (IgAN) has been reported to ameliorate the long-term prognosis of IgAN, but its mode of action has not been fully elucidated. In this study, we examined the effect of steroids on glomerular morphological changes in IgAN. Methods. We

examined 16 patients with biopsy-proven IgAN (male/female = 11/5, mean age 32.1 years) who were divided into prognosis groups according to criteria set by the Japanese Society of Nephrology. Initially, they received a loading dose of steroids, followed by a daily dose of 10-15 mg prednisolone. After 12 months, they underwent a second biopsy, and their histological and clinical features were examined. Results. Before and after therapy, systolic blood pressure, diastolic blood pressure, serum creatinine and creatinine clearance all remained unchanged. However, urinary protein excretion decreased dramatically, from 1.6±1.7 to 0.4±0.2 g/day (P<0.005). Furthermore, computerized imaging revealed a significant reduction of the mesangial matrix index (MMI) from 14.5±5.2 to 9.5±3.6% (P<0.001). The numbers of sclerosing glomeruli did not change. Conclusions. Steroid therapy reduces mesangial matrix accumulation and reduces urinary protein excretion in advanced IgAN.

CT Medical Descriptors:
*immunoglobulin A nephropathy: DI, diagnosis
*immunoglobulin A nephropathy: DT, drug therapy
kidney biopsy
prognosis
histopathology
clinical feature
systolic blood pressure
diastolic blood pressure
blood pressure monitoring
creatinine blood level
creatinine clearance
urinary excretion
image analysis
mesangium cell
extracellular matrix
glomerulosclerosis
disease severity
hypertension: CO, complication
hypertension: DT, drug therapy
proteinuria
infection: SI, side effect
stomach ulcer: SI, side effect
diabetes mellitus: SI, side effect
disease exacerbation: SI, side effect
human
male
female
clinical article
controlled study
human tissue
adult
article
priority journal
Drug Descriptors:
*methylprednisolone: AE, adverse drug reaction
*methylprednisolone: DO, drug dose
*methylprednisolone: DT, drug therapy
*methylprednisolone: PD, pharmacology
prednisolone: AE, adverse drug reaction
prednisolone: DO, drug dose
prednisolone: DT, drug therapy
prednisolone: PD, pharmacology
creatinine: EC, endogenous compound
steroid: AE, adverse drug reaction

steroid: DO, drug dose
steroid: DT, drug therapy
steroid: PD, pharmacology
calcium antagonist: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor
angiotensin 2 receptor antagonist
dilazep: DT, drug therapy
antithrombocytic agent: DT, drug therapy
RN (methylprednisolone) 6923-42-8, 83-43-2; (prednisolone) 50-24-8; (creatinine) 19230-81-0, 60-27-5; (dilazep) 20153-98-4, 35898-87-4

L67 ANSWER 66 OF 72 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003075271 EMBASE
TITLE: Association between vitamin D receptor gene polymorphisms and tubular citrate handling in calcium nephrolithiasis.
AUTHOR: Mossetti G.; Vuotto P.; Rendina D.; Numis F.G.; Viceconti R.; Giordano F.; Cioffi M.; Scopacasa F.; Nunziata V.
CORPORATE SOURCE: V. Nunziata, Dipto. di Med. Clin. e Sperimentale, Universita Federico II, via S. Pansini, 5, 80131 Naples, Italy. nunziata@unina.it
SOURCE: Journal of Internal Medicine, (1 Feb 2003) Vol. 253, No. 2, pp. 194-200.
Refs: 44
ISSN: 0954-6820 CODEN: JINMEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030227
Last Updated on STN: 20030227

AB Objectives. Hypocitraturia is a risk factor for calcium nephrolithiasis. 1.25(OH)(2)D(3) influences renal citrate handling and enhances citraturia. The aim of this study was to evaluate the relationship between vitamin D receptor (VDR) allelic variant and urinary citrate excretion in recurrent stone formers (SF) patients. Design. Case-control study. Subjects. A total of 220 recurrent calcium oxalate SF patients and 114 healthy control (C) subjects were enrolled for this study. Subjects with urinary tract infections, hyperparathyroidism, cystinuria >70 μmol/24 h, gouty diathesis, renal tubular acidosis, renal failure, chronic diarrhoeal states, intake of thiazide diuretics, **angiotensin**-converting enzyme (ACE)-inhibitors, glucocorticoids or oestrogens were excluded. A standard constant diet was given for 7 days. The 24-h urinary citrate excretion and the active tubular reabsorption of filtered citrate (Rcit) were evaluated. Hypocitraturia was defined as a urinary citrate excretion lower than 1.7 mmol day(-1). Stone formers patients and C were genotyped for BsmI and TaqI VDR alleles. Contingency table chi-square tests were used to compare genotype frequencies in hypocitraturic SF patients, normocitraturic SF and C. Results. The prevalence of hypocitraturia in SF patients was 32.7% (72 of 200). Hypocitraturia in these patients resulted from excessive Rcit of a normal load of citrate. We found a different distribution ($P < 0.05$) of BsmI and TaqI VDR genotypes in hypocitraturic SF patients compared with normocitraturic SF and C. In particular, the prevalence of bb and TT VDR genotypes in hypocitraturic SF was significantly higher than in normocitraturic SF and C. Conclusions. These results point to a genetic association between BsmI and TaqI VDR polymorphisms and idiopathic hypocitraturia in calcium-oxalate recurrent

SF patients.
CT Medical Descriptors:
*nephrolithiasis
DNA polymorphism
risk factor
urine level
allele
urinary tract infection
hyperparathyroidism
cystinuria
gout
kidney tubule acidosis
kidney failure
chronic diarrhea
standard
diet
kidney tubule absorption
genotype
chi square test
prevalence
genetic association
disease association
case control study
human
male
female
major clinical study
controlled study
adult
article
priority journal
Drug Descriptors:
*vitamin D receptor: EC, endogenous compound
*citric acid: EC, endogenous compound
*calcium: EC, endogenous compound
thiazide diuretic agent
dipeptidyl carboxypeptidase inhibitor
glucocorticoid
estrogen
calcium oxalate: EC, endogenous compound
RN (citric acid) 126-44-3, 5949-29-1, 77-92-9, 8002-14-0; (calcium) 7440-70-2; (calcium oxalate) 563-72-4

L67 ANSWER 67 OF 72 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002194944 EMBASE
TITLE: [Unrecognized causes of chronic cough].
CAUSES MECONNUES DE TOUX CHRONIQUE.
AUTHOR: Auliac J.B.; Bota S.; Nouvet G.
CORPORATE SOURCE: G. Nouvet, Clinique Pneumologique, CHRU de Rouen, Hopital C Nicolle, I rue de Germont, 76031 Rouen Cedex, France. georges.nouvet@chu-rouen.fr
SOURCE: Revue des Maladies Respiratoires, (2002) Vol. 19, No. 2 I, pp. 207-216.
Refs: 81
ISSN: 0761-8425 CODEN: RMREEY
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 20020620
Last Updated on STN: 20020620

AB Chronic cough is defined as persistence of the symptom for longer than one month. It is a common reason for consultation. A systematic diagnostic approach based on the history, clinical examination and a number of investigations (chest x-ray, lung function tests, oesophageal pH monitoring and sinus x-rays) reveals the cause in most cases. The main aetiologies are post-nasal drip, gastro-oesophageal reflex, asthma, chronic bronchitis, and the use of **angiotensin** converting enzyme inhibitors. Nevertheless, in some cases, the cause is not found. In this situation it is necessary to search for less common pathologies where cough is just a symptom of systemic disease, such as connective tissue disorder (Sjogren's syndrome, atrophic polychondritis), vasculitis (Wegener's granulomatosis), Horton's syndrome (cluster headaches), amyloidosis and **inflammatory bowel** disease. It may also be a matter of local pathology of the tracheo-bronchial tree, such as tracheo-bronchomegaly, tracheopathia osteoplastica, rare or unrecognized infections (whooping cough, post-viral cough, bronchial tuberculosis), reactive bronchial dysfunction, eosinophilic bronchitis or radiologically occult bronchial carcinoma. It is also necessary to consider vocal cord dysfunction and cough due to medication before accepting a diagnosis of psychogenic cough.

CT Medical Descriptors:
*coughing: ET, etiology
*coughing: SI, side effect
chronic disease: ET, etiology
chronic disease: SI, side effect
symptom
diagnostic approach route
anamnesis
clinical examination
diagnostic imaging
thorax radiography
lung function test
esophagus pH
pH measurement
gastroesophageal reflux
asthma
chronic bronchitis
drug use
connective tissue disease
Sjoegren syndrome
relapsing polychondritis
Wegener granulomatosis
temporal arteritis
vasculitis
amyloidosis
cluster headache
differential diagnosis
tracheobronchial tree
respiratory tract disease
respiratory tract infection
lung carcinoma
vocal cord paralysis
idiopathic disease

gastrointestinal disease
human
review
Drug Descriptors:
dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction

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ACCESSION NUMBER: 2001058753 EMBASE
TITLE: Characterization and clinical course of patients not receiving aspirin for acute myocardial infarction: Results from the MITRA and MIR studies.
AUTHOR: Frilling B.; Schiele R.; Gitt A.K.; Zahn R.; Schneider S.; Glunz H.-G.; Gieseler U.; Baumgartel B.; Asbeck F.; Senges J.
CORPORATE SOURCE: B. Frilling, Department of Cardiology, Bremserstr 79, 67063 Ludwigshafen, Germany. FrillinB@klilu.de
SOURCE: American Heart Journal, (2001) Vol. 141, No. 2, pp. 200-205.
Refs: 17
ISSN: 0002-8703 CODEN: AHJOA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010223
Last Updated on STN: 20010223

AB Background: Clinical trials have shown the efficacy of aspirin for acute myocardial infarction (AMI). However, not all patients receive aspirin for AMI. The aim of this study was to provide information on characteristics and clinical course of patients not treated with aspirin for AMI. Methods: We analyzed the data of the Myocardial Infarction Registry (MIR) and the Maximal Individual Therapy of Acute Myocardial Infarction (MITRA) registry. MITRA and MIR were prospective multicenter registries of patients with ST segment elevation myocardial infarction in Germany. Results: of 22,572 patients registered from 1994 to 1998, 1767 (7.8%) did not receive aspirin within the first 48 hours after admission. Multivariate analysis revealed two main factors associated with withholding aspirin for AMI: relative contraindications to aspirin (gastric ulcer [odds ratio (OR) 4.9, 95% confidence interval (CI) 3.7-5.7], renal insufficiency [OR 1.4, 95% CI 1.1-1.8]), and critical clinical state at admission (cardiogenic shock [OR 1.5, 95% CI 1.2-2.1] and prehospital resuscitation [OR 1.8, 95% CI 1.4-2.2]). In addition, these patients were significantly less likely to receive reperfusion therapy and adjunctive medical therapy such as β-blockers and **angiotensin**-converting enzyme inhibitors. In-hospital mortality after adjustment for baseline characteristics was 27.2% in patients without aspirin compared with 11.1% in patients treated with aspirin. Conclusions: Only a minority of AMI patients (7.8%) did not receive aspirin. Relative contraindications to aspirin and a critical clinical state at admission were the main factors associated with withholding aspirin for AMI. Even after adjustment for patient characteristics, the mortality of patients without aspirin was almost three times higher.

CT Medical Descriptors:
*heart infarction: DT, drug therapy
disease course
mortality

drug contraindication
stomach ulcer
kidney failure
patient coding
human
male
female
major clinical study
clinical trial
aged
adult
article
priority journal
Drug Descriptors:
*acetylsalicylic acid: CT, clinical trial
*acetylsalicylic acid: DT, drug therapy
beta adrenergic receptor blocking agent: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
tissue plasminogen activator: DT, drug therapy
streptokinase: DT, drug therapy
RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (tissue plasminogen activator) 105913-11-9; (streptokinase) 9002-01-1

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ACCESSION NUMBER: 1999023645 EMBASE
TITLE: Prostaglandin mediated gastric acid secretion inhibitory effect as a possible mechanism for the antiulcer effect of **angiotensin** converting enzyme inhibitor (**captopril**) in pylorus ligated rats.
AUTHOR: Rao S.P.; Murthy K.D.; Nayak B.S.; Sathiamoorthy S.S.
CORPORATE SOURCE: S.P. Rao, Department of Physiology, International Centre for Health Sci., Kasturba Medical College, Manipal - 576 119, India
SOURCE: Indian Journal of Pharmacology, (1998) Vol. 30, No. 6, pp. 385-389.
Refs: 29
ISSN: 0253-7613 CODEN: INJPD2
COUNTRY: India
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990204
Last Updated on STN: 19990204

AB Objective: To study the gastric secretory changes induced by antiulcer property of **captopril** and the role of prostaglandins in them. Methods: The effect of single dose of **captopril** and famotidine on different gastric parameters like ulcer index, pH, total acidity, mucopolysaccharide content and surface tension of gastric juice was studied by pyloric ligation alone and after pretreatment with ibuprofen. Results: **Captopril** and famotidine caused significant reduction in ulcer index and gastric acid secretion ($p<0.01$) when compared to saline control group. Both of them did not show any effect on mucus content and surface tension of gastric juice. Concurrent administration of ibuprofen reduced the anti-ulcer effect of **captopril** significantly ($P<0.01$) and nullified the acid secretion inhibitory effect of

captopril. However, the anti-ulcer and acid secretion inhibitory effects of famotidine were not altered by pretreatment with ibuprofen. Conclusion: **Captopril** may act through prostaglandins to inhibit gastric acid secretion and this effect of **captopril** on acid secretion may be the mechanism involved in its anti-ulcer effect.

CT Medical Descriptors:
***stomach ulcer: DT, drug therapy**
*stomach acid secretion
*pylorus ligation
prostaglandin metabolism
surface tension
stomach juice
drug effect
enzyme inhibition
stomach mucosa
stomach epithelium
stomach parietal cell
nonhuman
rat
animal experiment
animal model
controlled study
article
Drug Descriptors:
***captopril: DT, drug therapy**
***captopril: PD, pharmacology**
*famotidine: DT, drug therapy
*famotidine: PD, pharmacology
ibuprofen
dipeptidyl carboxypeptidase inhibitor

RN (**captopril**) **62571-86-2**; (famotidine) 76824-35-6; (ibuprofen) 15687-27-1

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ACCESSION NUMBER:	97145493 EMBASE
DOCUMENT NUMBER:	1997145493
TITLE:	Reliability of drug utilization evaluation as an assessment of medication appropriateness.
AUTHOR:	Shelton P.S.; Hanlon J.T.; Landsman P.B.; Scott M.A.; Lewis I.K.; Schmader K.E.; Samsa G.P.; Weinberger M.
CORPORATE SOURCE:	P.S. Shelton, School of Pharmacy, Campbell University, Dorothea Dix Hospital, 820 S. Boylan Ave., Raleigh, NC 27603, United States
SOURCE:	Annals of Pharmacotherapy, (1997) Vol. 31, No. 5, pp. 533-542. Refs: 43 ISSN: 1060-0280 CODEN: APHRER
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	020 Gerontology and Geriatrics 030 Pharmacology 037 Drug Literature Index 038 Adverse Reactions Titles
LANGUAGE:	English
SUMMARY LANGUAGE:	English; Spanish; French
ENTRY DATE:	Entered STN: 970604 Last Updated on STN: 970604

AB OBJECTIVE: To test the reliability of drug utilization evaluation (DUE)

applied to medications commonly used by the ambulatory elderly. METHODS: A DUE model was developed for four domains: (1) justification for use, (2) critical process indicators, (3) complications, and (4) clinical outcomes. DUE criteria specific to use in the elderly were developed for **angiotensin**- converting enzyme (ACE) inhibitors and histamine2 (H2)-antagonists, and consensus was reached by an external expert panel. After pilot testing, two clinical pharmacists independently evaluated these medications, applying the DUE criteria and rating each item as appropriate or inappropriate. Interrater and intrarater reliability was assessed by using κ statistics. RESULTS: In a sample of 208 ambulatory elderly veterans, 42 (20.2%) were taking an ACE inhibitor and 56 (26.9%) an H2' antagonist. The interrater agreement for individual domains, represented by κ statistics, were 0.10-0.58 and 0-0.83 for ACE inhibitors and H2-antagonists, respectively. The κ statistic for overall agreement, which considered ratings from all criteria across all domains, was 0.24 for ACE inhibitors and 0.18 for H2-antagonists. Intrarater reliability was assessed 3 months later, and κ statistics were 0.61-0.65 (0.49 overall) and 0-0.96 (0.81 overall) for ACE inhibitors and H2- antagonists, respectively. CONCLUSIONS: lntrarater reliability for DUE was good to excellent. However, interrater reliability exhibited only marginal reproducibility, particularly where evaluators were required to use subjective judgment (i.e., complications, clinical outcomes). DUE may not be a suitable standard for assessing medication appropriateness in ambulatory elderly patients.

CT Medical Descriptors:
*drug utilization
*geriatrics
*prescription
*treatment outcome
aged
article
congestive heart failure: DT, drug therapy
drug indication
duodenum ulcer: PC, prevention
duodenum ulcer: DT, drug therapy
esophagitis: DT, drug therapy
gastroesophageal reflux: DT, drug therapy
gastrointestinal symptom: SI, side effect
human
hypertension: DT, drug therapy
hypotension: SI, side effect
major clinical study
oral drug administration
priority journal
reliability
statistical analysis
stomach ulcer: PC, prevention
stomach ulcer: DT, drug therapy
Drug Descriptors:
***dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction**
***dipeptidyl carboxypeptidase inhibitor: DT, drug therapy**
***dipeptidyl carboxypeptidase inhibitor: PE, pharmacoeconomics**
*histamine h2 receptor antagonist: PE, pharmacoeconomics
*histamine h2 receptor antagonist: DT, drug therapy
*histamine h2 receptor antagonist: AE, adverse drug reaction
captopril: DT, drug therapy
captopril: PE, pharmacoeconomics
cimetidine: PE, pharmacoeconomics
cimetidine: DT, drug therapy

enalapril: DT, drug therapy
enalapril: PE, pharmacoeconomics
lisinopril: DT, drug therapy
lisinopril: PE, pharmacoeconomics
ranitidine: DT, drug therapy
ranitidine: PE, pharmacoeconomics
RN (**captopril**) **62571-86-2**; (cimetidine) 51481-61-9, 70059-30-2; (**enalapril**) **75847-73-3**; (**lisinopril**) **76547-98-3**, 83915-83-7; (ranitidine) 66357-35-5, 66357-59-3

L67 ANSWER 71 OF 72 EMBASE
ACCESSION NUMBER: 94151303 EMBASE
DOCUMENT NUMBER: 1994151303
TITLE: Understanding and treating Bartter syndrome.
AUTHOR: Gordon J.A.; Stokes III J.B.
CORPORATE SOURCE: Division of Nephrology, Department of Medicine, Univ. of Iowa College of Medicine,Iowa City, IA, United States
SOURCE: Hospital Practice, (1994) Vol. 29, No. 5, pp. 103-108+110. ISSN: 8750-2836 CODEN: HOPRBW
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940608
Last Updated on STN: 940608

AB Most of its clinical manifestations are the result of hypokalemia. The diagnosis is one of exclusion, mainly of surreptitious vomiting and diuretic abuse. The primary cause remains unknown but the most likely candidate is reduced sodium chloride reabsorption in the thick ascending limb of Henle's loop Current therapy focuses on multiple agents to reduce massive potassium loss.

CT Medical Descriptors:
*bartter syndrome: DT, drug therapy
*bartter syndrome: ET, etiology
*bartter syndrome: TH, therapy
*bartter syndrome: DI, diagnosis
aldosterone blood level
chloride transport
chronic diarrhea: DI, diagnosis
clinical feature
differential diagnosis
diuresis
drug intoxication: DI, diagnosis
henle loop
human
hypokalemia: TH, therapy
hypokalemia: ET, etiology
hypokalemia: DT, drug therapy
hypokalemia: DI, diagnosis
magnesium deficiency: DI, diagnosis
pathophysiology
plasma renin activity
potassium urine level

prostaglandin synthesis
renin angiotensin aldosterone system
review
sodium absorption
vomiting: DI, diagnosis
Drug Descriptors:
*loop diuretic agent: PD, pharmacology
*loop diuretic agent: DT, drug therapy
*loop diuretic agent: CM, drug comparison
*loop diuretic agent: CB, drug combination
*potassium ion: EC, endogenous compound
*potassium sparing diuretic agent: CM, drug comparison
*potassium sparing diuretic agent: CB, drug combination
*potassium sparing diuretic agent: DT, drug therapy
*potassium sparing diuretic agent: PD, pharmacology
*prostaglandin synthase inhibitor: PD, pharmacology
*prostaglandin synthase inhibitor: CB, drug combination
*prostaglandin synthase inhibitor: CM, drug comparison
*prostaglandin synthase inhibitor: DT, drug therapy
*sodium chloride: PK, pharmacokinetics
aldosterone: EC, endogenous compound
aldosterone: PD, pharmacology
amiloride: CB, drug combination
amiloride: PD, pharmacology
amiloride: DT, drug therapy
amiloride: CM, drug comparison
aminoglycoside antibiotic agent: TO, drug toxicity
angiotensin: PD, pharmacology
angiotensin: EC, endogenous compound
dipeptidyl carboxypeptidase inhibitor: CB, drug combination
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
ibuprofen: DT, drug therapy
ibuprofen: PD, pharmacology
ibuprofen: CM, drug comparison
ibuprofen: CB, drug combination
indometacin: PD, pharmacology
indometacin: CB, drug combination
indometacin: CM, drug comparison
indometacin: DT, drug therapy
potassium chloride: DT, drug therapy
potassium chloride: PD, pharmacology
potassium chloride: CM, drug comparison
potassium chloride: CB, drug combination
prostaglandin e2: EC, endogenous compound
prostaglandin e2: PD, pharmacology
prostaglandin synthase: EC, endogenous compound
renin: PD, pharmacology
renin: EC, endogenous compound
spironolactone: PD, pharmacology
spironolactone: DT, drug therapy
spironolactone: CM, drug comparison
spironolactone: CB, drug combination
triamterene: PD, pharmacology
triamterene: DT, drug therapy
triamterene: CM, drug comparison
triamterene: CB, drug combination
RN (potassium ion) 24203-36-9; (sodium chloride) 7647-14-5; (aldosterone)

52-39-1, 6251-69-0; (amiloride) 2016-88-8, 2609-46-3; (**angiotensin**) 11128-99-7, 1407-47-2; (ibuprofen) 15687-27-1; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (potassium chloride) 7447-40-7; (prostaglandin e2) 363-24-6; (prostaglandin synthase) 39391-18-9, 59763-19-8, 9055-65-6; (renin) 61506-93-2, 9015-94-5; (spironolactone) 52-01-7; (triamterene) 396-01-0

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ACCESSION NUMBER: 86211290 EMBASE
DOCUMENT NUMBER: 1986211290
TITLE: Gastrointestinal complications in critically ill patients: The intensivists' overview.
AUTHOR: Gottlieb J.E.; Menashe P.I.; Cruz E.
CORPORATE SOURCE: Yale University School of Medicine, Norwalk Hospital, Norwalk, CT, United States
SOURCE: American Journal of Gastroenterology, (1986) Vol. 81, No. 4, pp. 227-238.
CODEN: AJGAAR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
048 Gastroenterology
006 Internal Medicine
024 Anesthesiology
009 Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB The critical care environment may be characterized by invasive monitoring, vasoactive drugs, and major interventions which may have adverse effects on gastrointestinal function. Furthermore, conditions such as heart failure or sepsis may compromise oxygen delivery to gastrointestinal organs. Life threatening illness from a variety of causes may produce endoscopically evident gastritis or ulceration in up to 100% of patients, and clinically evident bleeding in 20%. Clinicial studies suggest that antacids or H2 receptor blockers may reduce the frequency of this complication. Other conditions are associated with a spectrum of hepatic dysfunction ranging from the cholestatic jaundice of reactive hepatopathy during sepsis to centrilobular necrosis and hepatitis of shock liver. Additionally, many drugs used in the critical care setting may adversely affect mesenteric oxygen delivery and result in ischemia or infarction of the bowel. An increased awareness and understanding of these and other gastrointestinal complications in critically ill patients will, it is hoped, lead to earlier detection and better therapy than is now available.

CT Medical Descriptors:
*adverse drug reaction
*cholecystitis
*confusion
*gastritis
*gastrointestinal symptom
*gastrointestinal toxicity
*gastroscopy
*intensive care
*intestine infarction
*intestine ischemia
*liver failure
*liver toxicity

*neurotoxicity
*shock
*stomach acid secretion
***stomach ulcer**
*stress ulcer
heart failure
jaundice
sepsis
survey
priority journal
digestive system
intoxication
psychological aspect
nervous system
stomach
cardiovascular system
liver
gallbladder
review
human
peripheral vascular system
large intestine
small intestine
diagnosis
heart
Drug Descriptors:
*adrenalin
*aminophylline
***angiotensin**
*antacid agent
*antihistaminic agent
*arbaprostil
*benzodiazepine derivative
***captopril**
*carbenoxolone
*cholinergic receptor blocking agent
*cimetidine
*digoxin
*dopamine
*growth hormone
*histamine
*histamine h2 receptor
*histamine h2 receptor antagonist
*isoprenaline
*metaraminol
*methoxamine
*nitroprusside sodium
*noradrenalin
*oxygen
*pentagastrin
*phenylephrine
*propranolol
*prostaglandin e2
*retinol
*vasoactive agent
*vasoconstrictor agent
RN (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (aminophylline) 317-34-0; (**angiotensin**) 11128-99-7, 1407-47-2; (arbaprostil) 55028-70-1; (**captopril**) **62571-86-2**; (carbenoxolone) 5697-56-3,

7421-40-1; (cimetidine) 51481-61-9, 70059-30-2; (digoxin) 20830-75-5, 57285-89-9; (dopamine) 51-61-6, 62-31-7; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (histamine) 51-45-6, 56-92-8, 93443-21-1; (isoprenaline) 299-95-6, 51-30-9, 6700-39-6, 7683-59-2; (metaraminol) 33402-03-8, 54-49-9; (methoxamine) 390-28-3, 61-16-5; (nitroprusside sodium) 14402-89-2, 15078-28-1; (noradrenalin) 1407-84-7, 51-41-2; (oxygen) 7782-44-7; (pentagastrin) 5534-95-2; (phenylephrine) 532-38-7, 59-42-7, 61-76-7; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (prostaglandin e2) 363-24-6; (retinol) 68-26-8, 82445-97-4